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<p>(21) International Application Number: PCT/US94/03852</p> <p>(22) International Filing Date: 5 April 1994 (05.04.94)</p> <p>(30) Priority Data:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 30%;">08/043,212</td> <td style="width: 40%;">5 April 1993 (05.04.93)</td> <td style="width: 30%;">US</td> </tr> <tr> <td>08/120,169</td> <td>10 September 1993 (10.09.93)</td> <td>US</td> </tr> <tr> <td>08/166,308</td> <td>10 December 1993 (10.12.93)</td> <td>US</td> </tr> </table> <p>(60) Parent Applications or Grants</p> <p>(63) Related by Continuation</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 30%;">US</td> <td style="width: 40%;">08/043,212 (CIP)</td> <td style="width: 30%;"></td> </tr> <tr> <td>Filed on</td> <td>5 April 1993 (05.04.93)</td> <td></td> </tr> <tr> <td>US</td> <td>08/120,169 (CIP)</td> <td></td> </tr> <tr> <td>Filed on</td> <td>10 September 1993 (10.09.93)</td> <td></td> </tr> <tr> <td>US</td> <td>08/166,308 (CIP)</td> <td></td> </tr> <tr> <td>Filed on</td> <td>10 December 1993 (10.12.93)</td> <td></td> </tr> </table> <p>(71) Applicant (for all designated States except US): SYNAPTIC PHARMACEUTICAL CORPORATION [US/US]; 215 College Road, Paramus, NJ 07652 (US).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): GLUCHOWSKI, Charles [US/US]; 153 Chopin Drive, Wayne, NJ 07470 (US). WET-</p>		08/043,212	5 April 1993 (05.04.93)	US	08/120,169	10 September 1993 (10.09.93)	US	08/166,308	10 December 1993 (10.12.93)	US	US	08/043,212 (CIP)		Filed on	5 April 1993 (05.04.93)		US	08/120,169 (CIP)		Filed on	10 September 1993 (10.09.93)		US	08/166,308 (CIP)		Filed on	10 December 1993 (10.12.93)		<p>ZEL, John, M. [US/US]; 72B Miles Street, Elmwood Park, NJ 07407 (US). CHIU, George [CN/US]; 13 Kelly Court, Bridgewater, NJ 08807 (US). MARZABADI, Mohammad, R. [IR/US]; Apartment F7, 49 Finnigan Avenue, Saddle Brook, NJ 07662 (US). WONG, Wai, C. [GB/US]; Apartment C, 104 Reservoir Avenue, River Edge, NJ 07661 (US). NAGARATHNAM, Dhanapalan [IN/US]; Apartment 74, 450 Island Road, Ramsey, NJ 07446 (US).</p> <p>(74) Agent: WHITE, John, P.; Cooper & Dunham, 30 Rockefeller Plaza, New York, NY 10112 (US).</p> <p>(81) Designated States: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published Without international search report and to be republished upon receipt of that report.</p>	
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<p>(54) Title: DIHYDROPYRIDINES AND NEW USES THEREOF</p> <p>(57) Abstract</p> <p>The invention provides a method of treating benign prostatic hyperplasia in a subject which comprises administering to the subject a therapeutically effective amount of a compound having structure (I) wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_b-O-(CH_2)_k-$, where b and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_b-CH=CH-(CH_2)_k-$; or $-(CH_2)_b-C\equiv C-(CH_2)_k-$, where b and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is 0, NH, or CH₂; wherein R¹ is a linear or branched chain alkyl, alkoxyalkyl or arylalkyl group; wherein R² and R⁴ are independently the same or different and are H, or a linear or branched chain alkyl group; wherein R³ is H, a linear or branched chain alkyl, alkoxy, alkoxyalkyl or acyl group; and wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, F, NO₂, CN, CF₃, or NH₂, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone, or mono- or dialkylamino group. Other active compounds containing one, two or three rings are also disclosed as well as pharmaceutical compositions prepared therefrom and methods of use in the treatment of BPH, inhibition of cholesterol synthesis, and reduction of intraocular pressure.</p>																														
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Dihydropyridines and New Uses Thereof

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This application is a continuation-in-part of U.S. Serial No. 08/166,308, filed December 10, 1993, which is a continuation-in-part of U.S. Serial No. 08/120,169, filed September 10, 1993, which is a continuation-in-part of
10 U.S. Serial No. 08/043,212, filed April 5, 1993, the contents of which are hereby incorporated by reference into this application.

Background of the Invention

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Benign Prostatic Hyperplasia (BPH), also called Benign Prostatic Hypertrophy, is a progressive condition which is characterized by a nodular enlargement of prostatic tissue resulting in obstruction of the urethra. This
20 results in increased frequency of urination, nocturia, a poor urine stream and hesitancy or delay in starting the urine flow. Chronic consequences of BPH can include hypertrophy of bladder smooth muscle, a decompensated bladder and an increased incidence of urinary tract
25 infection. The specific biochemical, histological and pharmacological properties of the prostate adenoma leading to the bladder outlet obstruction are not yet known. However, the development of BPH is considered to be an inescapable phenomenon for the aging male
30 population. BPH is observed in approximately 70% of males over the age of 70. Currently, in the United States, the method of choice for treating BPH is surgery (Lepor, H., Urol. Clinics North Amer., 17, 651 (1990)). Over 400,000 prostatectomies are performed annually (data
35 from 1986). A medicinal alternative to surgery is clearly very desirable. The limitations of surgery for treating BPH include the morbidity rate of an operative

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procedure in elderly men, persistence or recurrence of obstructive and irritative symptoms, as well as the significant cost of surgery.

- 5 α -Adrenergic receptors are specific neuroreceptor proteins located in the peripheral and central nervous systems on tissues throughout the body. These receptors are important switches for controlling many physiological functions and, thus, represent important targets for drug
10 development. In fact, many α -adrenergic drugs have been developed over the past 40 years. Examples include clonidine, phenoxybenzamine and prazosin (treatment of hypertension), naphazoline (nasal decongestant), and apraclonidine (treating glaucoma). α -Adrenergic drugs
15 can be broken down into two distinct classes: agonists (clonidine and naphazoline are agonists), which mimic the receptor activation properties of the endogenous neurotransmitter norepinephrine, and antagonists (phenoxybenzamine and prazosin are antagonists), which
20 act to block the effects of norepinephrine. Many of these drugs are effective but also produce unwanted side effects (for example, clonidine produces dry mouth and sedation in addition to its antihypertensive effects).
- 25 During the past 15 years a more precise understanding of α -adrenergic receptors and their drugs has evolved through increased scientific scrutiny. Prior to 1977, only one α -adrenergic receptor was known to exist. Between 1977 and 1988, it was accepted by the scientific
30 community that at least two α -adrenergic receptors-- α_1 and α_2 --existed in the central and peripheral nervous systems. Since 1988, new techniques in molecular biology have led to the identification of at least six α -adrenergic receptors which exist throughout the central and
35 peripheral nervous systems: α_{1A} , α_{1B} , α_{1C} , α_{2A} , α_{2B} and α_{2C} (Bylund, D.B., FASEB J., 6, 832 (1992)). It is not known precisely which physiological responses in the body are

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controlled by each of these receptors. In addition, many α -adrenergic drugs that were developed before 1992 are not selective for any particular α -adrenergic receptor. Many of these drugs produce untoward side effects which
5 may be attributed to their poor α -adrenergic receptor selectivity.

Since the mid 1970's, nonselective α -antagonists have been prescribed to treat BPH. In 1976, M. Caine, et al.
10 (Brit. J. Urol., 48, 255 (1976)), reported that the nonselective α -antagonist phenoxybenzamine was useful in relieving the symptoms of BPH. This drug may produce its effects by interacting with α -receptors located on the prostate. However, this drug also produces significant
15 side effects which severely limit its use in treating patients on a chronic basis. More recently, the α -adrenergic antagonists prazosin and terazosin have also been found to be useful for treating BPH. However, these drugs also produce untoward side effects.

20 This invention relates to uses for dihydropyridine derivatives previously reported in Flockerzi, D., et. al., US Patent 4,707,486, issued November 17, 1987, and Zimmerman, P., et.al., PCT International Patent Application
25 WO 91/09846, published July 11, 1991, including methods of treatment of BPH. This invention also relates to novel dihydropyridine derivatives. This invention further relates to potent and selective alpha 1C antagonists without significant calcium channel activity.
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Brief Description of the Drawings

A more complete understanding of the invention and many of its advantages will become apparent by reference to the detailed description which follows when considered in
5 conjunction with the accompanying drawings, wherein:

Figure 1 illustrates condensation to form dihydro-pyridines by Reaction Scheme 1 (Method A).

10 Figure 2 illustrates condensation to form dihydro-pyridines by Reaction Scheme 2 (Method B).

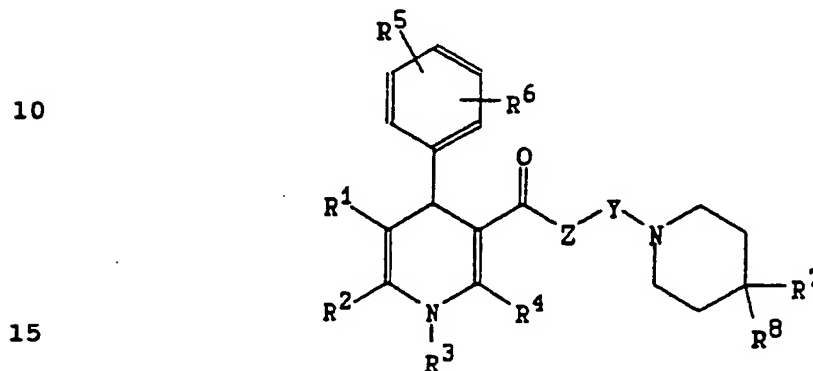
Figure 3 illustrates condensation to form dihydro-pyridines by Reaction Scheme 3 (Method C).
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Figure 4 illustrates condensation to form dihydro-pyridines by Reaction Scheme 4 (Method D).

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Summary of the Invention

The present invention provides a method of treating benign prostatic hyperplasia in a subject which comprises
 5 administering to the subject a therapeutically effective amount of a compound having the structure:

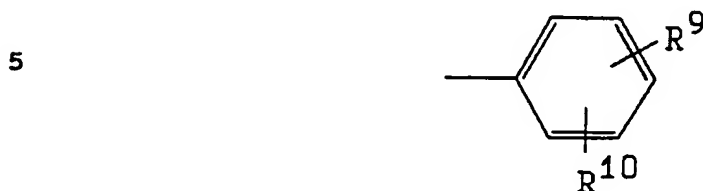


wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH or CH₂; wherein R¹ is a linear or branched chain alkyl, alkoxyalkyl or arylalkyl group; wherein R² and R⁴ are independently the same or different and are H, or a
 25 linear or branched chain alkyl group; wherein R³ is H, a linear or branched chain alkyl, alkoxy, alkoxyalkyl or acyl group; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, N₃, CN, CF₃, or NH₂, or a linear or branched chain alkyl, alkoxy, alkoxyalkyl, acyl, alkylsulfoxide, alkylsulfone or
 30 mono- or dialkylamino group; and wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR, OCOR, NH₂, NHR, NR₂, or NHCOR, where R is a linear chain alkyl group, a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,

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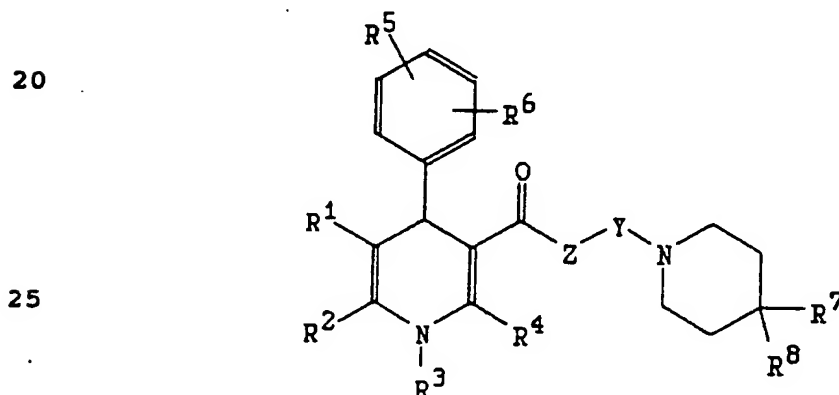
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quinolinyl, isoquinolinyl, pyrrolyl, furyl, or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, F, OH, OR', OCOR', OCOOR', OCONHR',
 NH₂, NHR', NR', NHCOR', NHCOOR' or NHCONHR', where R' is
 a linear or branched chain alkyl group.

The invention still further provides a method of treating
 15 diseases mediated by α_1 receptors in a subject which
 comprises administering to the subject a therapeutically
 effective amount of a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-$
 O $-(CH_2)_k-$, where h and k are independently the same or
 30 different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the
 same or different and are 1, 2, 3 or 4; wherein Z is O,
 NH, NCHO, NCOR, NR, NOR or CH₂, where R is a methyl, ethyl
 or propyl group; wherein R¹ is a linear or branched chain
 35 alkyl, alkoxyalkyl or arylalkyl group; wherein R² and R⁴
 are independently the same or different and are H, or a
 linear or branched chain alkyl group; wherein R³ is H, a

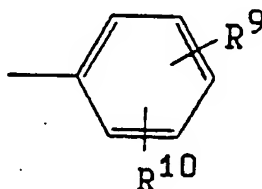
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linear or branched chain alkyl, alkoxy, alkoxyalkyl or acyl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, F, NO_2 , CN, CF_3 or NH_2 , or a linear or branched chain alkyl, alkoxy, alkoxy-

5 carbonyl, acyl, alkylsulfoxide, alkylsulfone or mono- or dialkylamino group; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR'' , $OCOR''$, NH_2 , NHR'' , NR'' , or $NHCOR''$, where R'' is a linear chain alkyl group, a benzyl group, a linear or

10 branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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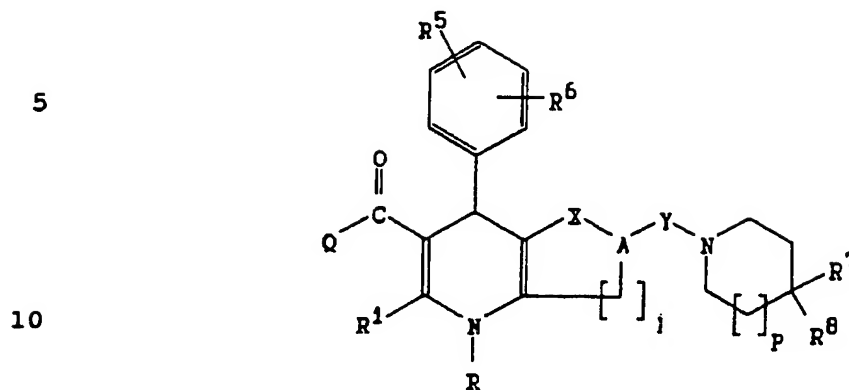


20 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, F, OH, OR''' , $OCOR'''$, $OCOOR'''$, $OCONHR'''$, NH_2 , NHR''' , NR''' , $NHCOR'''$, $NHCOOR'''$ or $NHCONHR'''$, where R''' is a linear or branched chain alkyl group.

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The invention further provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R

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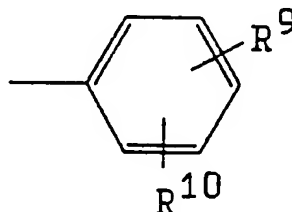
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is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R'₃Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R'₃Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein X is C=O, CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, N₃ or CF₃, or a

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linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone, or mono- or dialkyl-amino group, or together constitute a methylenedioxy group; wherein A is CH; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein j is 1 or 2; wherein p is 0, 1 or 2; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

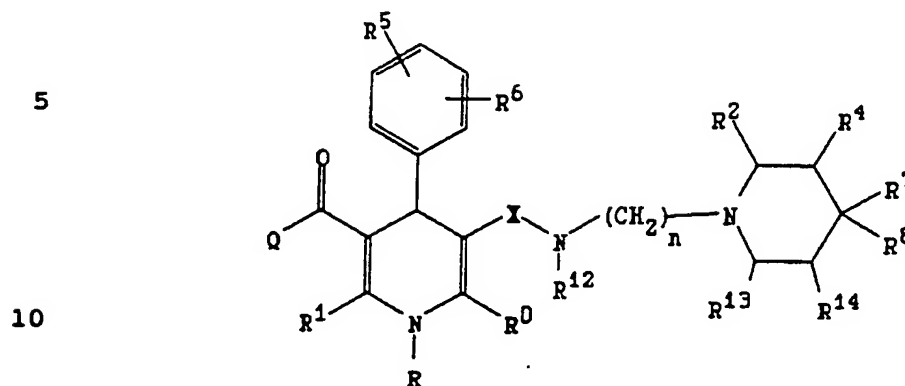
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

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The invention further provides a compound having the structure:



wherein X is C=O, CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Q

15 is OH, OR'', SH, SR''', NH₂, NHR''', NR''', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl

20 group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an

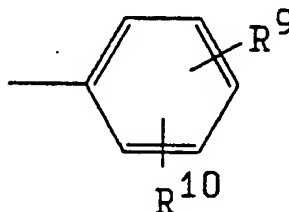
25 alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_vW, where W is NH₂, NHR', NR'₂, NHOH, N⁺R₃Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or

30 an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR'₂, NHOH, N⁺R₃Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z

35 is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H, a linear or branched chain alkyl or acyl group, or an

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aryl group; wherein R^2 , R^{13} , and R^{14} are independently the same or different and are H, or a linear or branched chain alkyl, hydroxyalkyl, alkoxyalkyl, amino alkyl, or aryl group; wherein R^4 is a linear or branched chain alkyl, alkoxyalkyl, hydroxyalkyl, or a linear or branched chain alkenylalkyl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , N_3 , CF_3 , a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

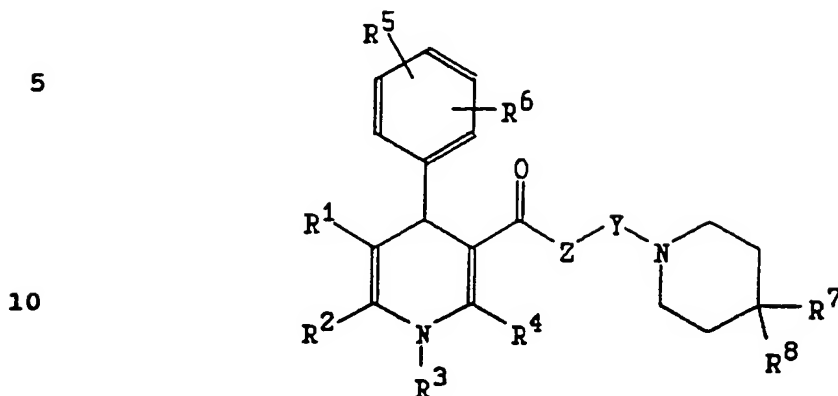


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

A general objective of the invention is to provide a method of treating diseases mediated by α_1 receptors in a subject which comprises administering to the subject a

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therapeutically effective amount of a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4, or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3, or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3, or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR, or CH₂, where R is a methyl, ethyl, or propyl group; wherein R¹ is a linear or branched chain alkyl, alkoxyalkyl, or arylalkyl group; wherein R² and R⁴ are independently the same or different and are H, or a linear or branched chain alkyl group; wherein R³ is H, a linear or branched chain alkyl, alkoxy, alkoxyalkyl, or acyl group; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, F, NO₂, CN, CF₃, or NH₂, or a linear or branched chain alkyl, alkoxy, alkoxyalkyl, acyl, alkylsulfoxide, alkylsulfone, or mono- or dialkylamino group; and wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR'', OCOR'', NH₂, NHR'', NR'', or NHCOR'', where R'' is a linear chain alkyl group, a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl,

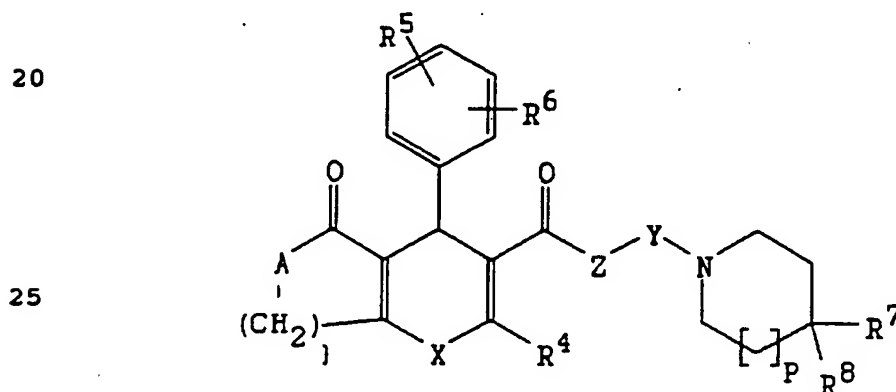
-13-

or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, F, OH, OR''' , $OCOR'''$, $OCOOR'''$, $OCONHR'''$, NH_2 , NHR''' , NR'''_2 , $NHCOR'''$, $NHCOOR'''$, $NHCONHR'''$, where R''' is a linear or branched chain alkyl group.

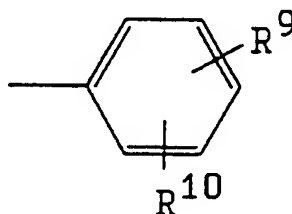
15 In addition, the present invention provides a compound useful for the treatment of benign prostatic hyperplasia and other disorders having the structure:



wherein A and X are independently the same or different
 30 and are CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O, or S, where R is a methyl, ethyl, or propyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4, or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3, or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$
 35 where h and k are independently the same or different and are 1, 2, 3, or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR', or CH_2 , where R' is a methyl, ethyl, or propyl

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group; wherein j is 1 or 2; wherein p is 0, 1, or 2; wherein R^4 is H, or a linear or branched chain, or cyclic alkyl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , or
 5 CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxy-carbonyl, acyl, alkylsulfoxide, alkylsulfone, or mono- or dialkylamino group, or together constitute a methylene-dioxy group; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR'' , $OCOR''$,
 10 NH_2 , NHR'' , NR'' , or $NHCOR''$, where R'' is a linear chain alkyl group, a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl, or thiophene group, or an
 15 aryl group having the structure:



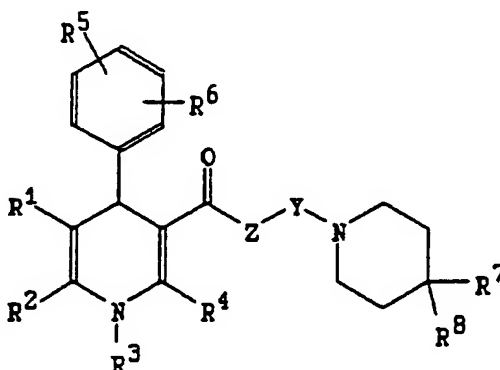
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, F, OH, OR''' , $OCOR'''$, $OCOOR'''$, $OCONHR'''$, NH_2 , NHR''' , NR''' , $NHCOR'''$, $NHCOOR'''$,
 25 $NHCONHR'''$, where R''' is a linear or branched chain alkyl group.

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Detailed Description of the Invention

The present invention provides a method of treating benign prostatic hyperplasia in a subject which comprises administering to the subject a therapeutically effective amount of a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH or CH₂; wherein R¹ is a linear or branched chain alkyl, alkoxyalkyl or arylalkyl group; wherein R² and R⁴ are independently the same or different and are H, or a linear or branched chain alkyl group; wherein R³ is H, a linear or branched chain alkyl, alkoxy, alkoxyalkyl or acyl group; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, N₃, CN, CF₃, or NH₂, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone or mono- or dialkylamino group; and wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR, OCOR, NH₂, NHR, NR₂, or NHCOR, where R is a linear chain alkyl group, a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,

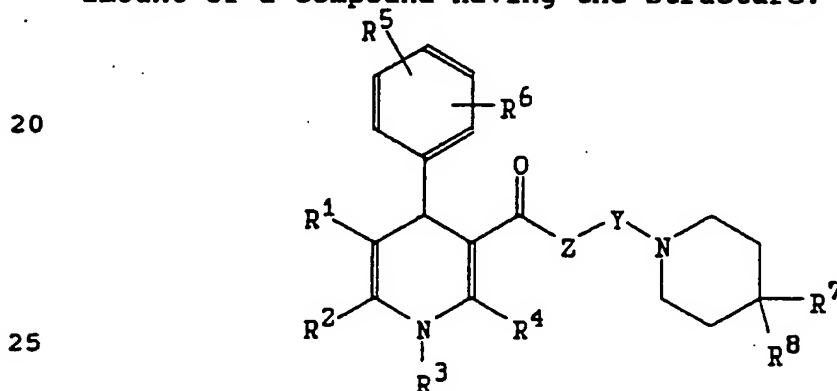
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quinolinyl, isoquinolinyl, pyrrol, furyl, or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, F, OH, OR' , $OCOR'$, $OCOOR'$, $OCONHR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $NHCOOR'$ or $NHCONHR'$, where R' is a linear or branched chain alkyl group.

The invention also provides a method of lowering
 15 intraocular pressure in a subject which comprises administering to the subject a therapeutically effective amount of a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-$ $O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or -
 30 $(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^1 is a linear or branched chain alkyl, alkoxyalkyl or arylalkyl group; wherein R^2 and R^4
 35 are independently the same or different and are H, or a linear or branched chain alkyl group; wherein R^3 is H, a linear or branched chain alkyl, alkoxy, alkoxyalkyl or

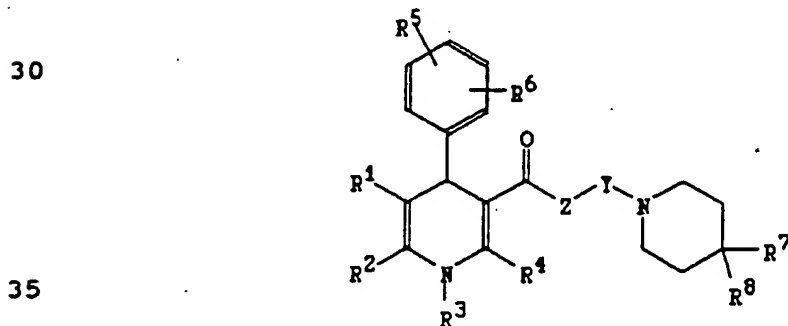
-17-

acyl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , N_3 , CN, CF_3 , or NH_2 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone or
 5 mono- or dialkylamino group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , or NHCOR' , where R' is a linear chain alkyl group, or a benzyl group, or are a linear or branched chain alkyl or cycloalkyl group, a
 10 heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



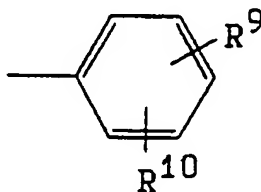
wherein R^9 and R^{10} are independently the same or different
 20 and are H, Cl, Br, F, OH, OR'' , OCOR'' , OCOOR'' , OCONHR'' , NH_2 , NHR'' , NR''_2 , NHCOR'' , NHCOOR'' or $\text{NHCONHR}''$, where R'' is a linear or branched chain alkyl group.

25 The invention further provides a method of inhibiting cholesterol synthesis in a subject which comprises administering to the subject a therapeutically effective amount of a compound having the structure:



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wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$ where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein R¹ is a linear or branched chain alkyl, alkoxyalkyl or arylalkyl group; wherein R² and R⁴ are independently the same or different and are H, or a linear or branched chain alkyl group; wherein R³ is H, a linear or branched chain alkyl, alkoxy, alkoxyalkyl or acyl group; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, F, NO_2 , CN, CF_3 , or NH_2 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone or mono- or dialkylamino group; and wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF_3 , OH, OR'' , OCOR'' , NH_2 , NHR'' , NR''_2 , or NHCOR'' , where R'' is a linear chain alkyl group, a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

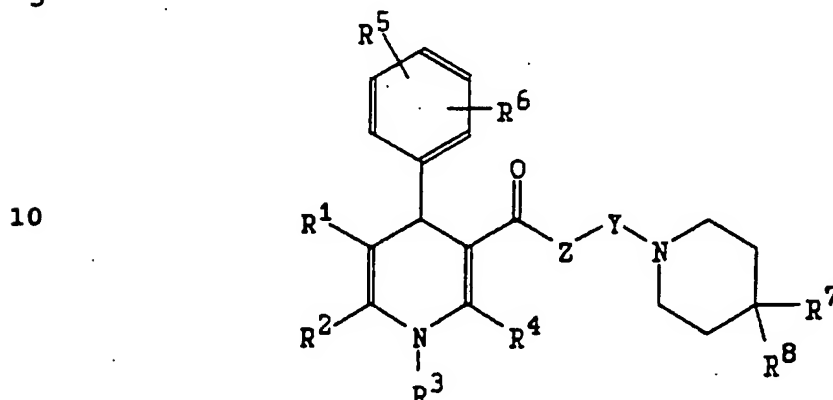


wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, F, OH, OR''' , OCOR''' , OCOOR''' , OCONHR''' , NH_2 , NHR''' , NR'''_2 , NHCOR''' , NHCOOR''' or $\text{NHCONHR}'''$, where R''' is a linear or branched chain alkyl group.

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The invention still further provides a method of treating diseases mediated by α_1 receptors in a subject which comprises administering to the subject a therapeutically effective amount of a compound having the structure:

5



- 15 wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-$
 $O-(CH_2)_k-$, where h and k are independently the same or
different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the
same or different and are 1, 2, 3 or 4; wherein Z is O,
20 NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl
or propyl group; wherein R^1 is a linear or branched chain
alkyl, alkoxyalkyl or arylalkyl group; wherein R^2 and R^4
are independently the same or different and are H, or a
linear or branched chain alkyl group; wherein R^3 is H, a
25 linear or branched chain alkyl, alkoxy, alkoxyalkyl or
acyl group; wherein R^5 and R^6 are independently the same
or different and are H, OH, Cl, Br, F, NO_2 , CN, CF_3 or NH_2 ,
or a linear or branched chain alkyl, alkoxy, alkoxy-
carbonyl, acyl, alkylsulfoxide, alkylsulfone or mono-or
30 dialkylamino group; and wherein R^7 and R^8 are independ-
ently the same or different and are H, CN, CF_3 , OH, OR'' ,
 $OCOR''$, NH_2 , NHR'' , NR'' , or $NHCOR''$, where R'' is a
linear chain alkyl group, a benzyl group, a linear or
branched chain alkyl or cycloalkyl group, or are a
35 heteroaryl group comprising a pyridyl, indolyl,

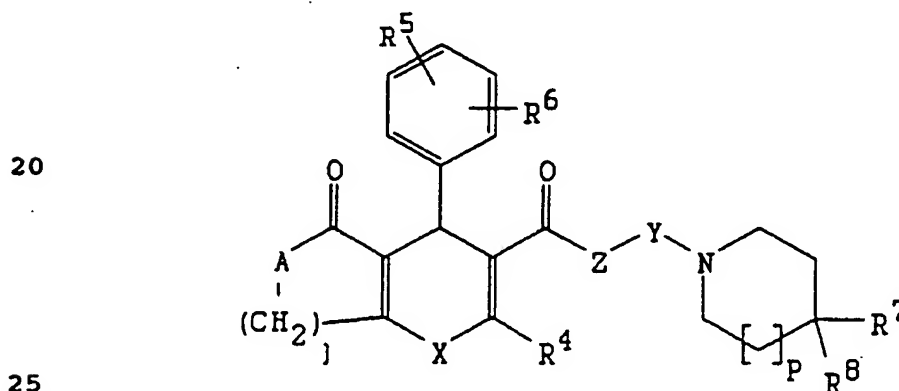
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indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 10 and are H, Cl, Br, F, OH, OR''', OCOR''', OCOOR''',
 OCONHR''', NH₂, NHR''', NR'''₂, NHCOR''', NHCOOR''' or
 NHCONHR''', where R''' is a linear or branched chain
 alkyl group.

15 The invention provides a compound having the structure:

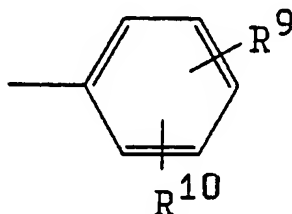


wherein A and X are independently the same or different
 and are CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S, where
 R is a methyl, ethyl or propyl group; wherein Y is
 30 -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-,
 where h and k are independently the same or different and
 are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-,
 where h and k are independently the same or different and
 are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR',
 35 NOR' or CH₂, where R' is a methyl, ethyl or propyl group;
 wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R⁴ is
 H, a linear, cyclic or branched chain alkyl, an

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alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-
 alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl
 or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR'_2 ,
 $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2 W^0 (CH_2)_v W^1$, or a linear
 5 or branched chain alkyl group, or an arylalkyl group, or
 an alkenyl or alkynyl group, or an aryl group, where R'
 is a linear or branched chain alkyl group, or an aryl
 group, where W^0 is O, S or NH, W^1 is NH_2 , NHR' , NR'_2 , $NHOH$,
 $N^+R'_3 Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or
 10 branched chain alkyl group, or an aryl group, where Z^- is
 a pharmaceutically acceptable counterion, and t is 1, 2,
 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^5 and R^6
 are independently the same or different and are H, OH,
 Cl, Br, I, F, NO_2 , CN, NH_2 , N_3 or CF_3 , or a linear or
 15 branched chain alkyl, alkoxy, alkoxycarbonyl, acyl,
 alkylsulfoxide, alkylsulfone, or mono- or dialkylamino
 group, or together constitute a methylenedioxy group;
 wherein R^7 and R^8 are independently the same or different
 and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 ,
 20 $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' ,
 $COSH$, $COSR'$, $COO(CH_2)_q OH$ or $COO(CH_2)_q OR'$, or a benzyl
 group, a linear or branched chain alkyl or cycloalkyl
 group, or are a heteroaryl group comprising a pyridyl,
 indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,
 25 furyl or thiophene group, or an aryl group having the
 structure:

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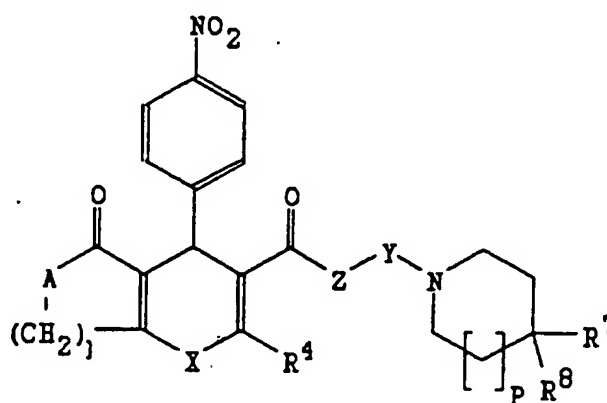
wherein R^9 and R^{10} are independently the same or different
 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$,
 35 $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where
 R' is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4

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or 5. As used herein, the term "pharmaceutically acceptable counterion" shall refer to any anion present in or compatible with mammalian tissue physiology, and includes among others chloride, bromide, iodide, acetate, carbonate, bicarbonate, tartrate, citrate, ascorbate, succinate, maleate, lactate, phosphate, sulfate, hydrogen phosphate, hydrogen sulfate or benzoate. In one embodiment, the invention provides a compound having the structure:

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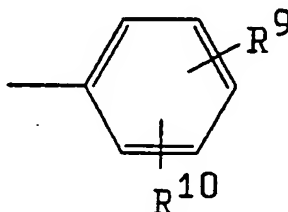
wherein A and X are independently the same or different and are CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein p is 0, 1 or 2; wherein R^4 is H, a linear, cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(\text{CH}_2)_q\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 , or $\text{CH}_2\text{W}^0(\text{CH}_2)_q\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain

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alkyl group, or an aryl group, where W^0 is O, S or NH, W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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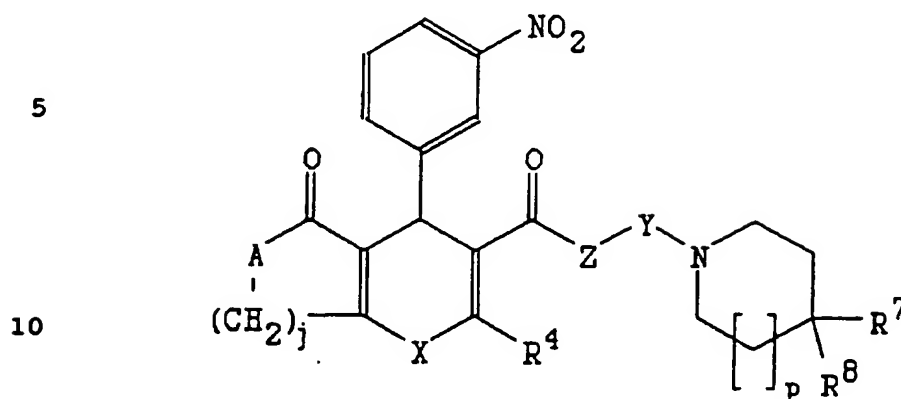
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4

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or 5. In another embodiment, the invention provides a compound having the structure:



wherein A and X are independently the same or different and are CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S, where

15 R is a methyl, ethyl or propyl group; wherein Y is - (CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and

20 are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0 or 2; wherein R⁴ is H, a linear, cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl,

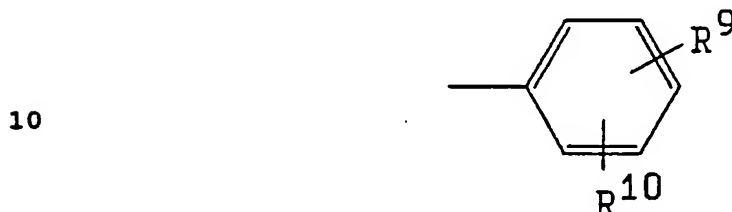
25 trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear

30 or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3,

35 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR',

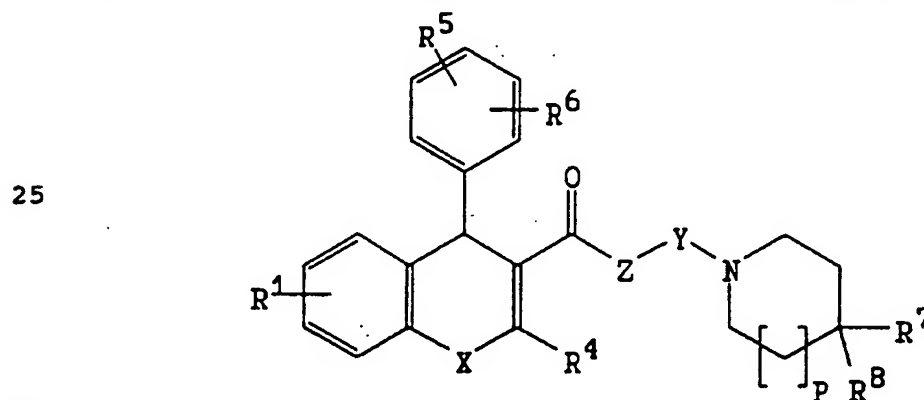
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CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or
 COO(CH₂)_qOR', or a benzyl group, a linear or branched
 chain alkyl or cycloalkyl group, or are a heteroaryl
 group comprising a pyridyl, indolyl, indolylalkyl,
 5 quinoliny, isoquinoliny, pyrrol, furyl or thiophene
 group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 and are H, Cl, Br, I, F, OH, NO₂, N₃, ORⁿ, OCORⁿ, OCOORⁿ,
 15 OCONHRⁿ, NH₂, NHRⁿ, NRⁿ, NHCORⁿ, NHCOORⁿ or NHCONHRⁿ, where
 R' is a linear or branched chain alkyl group, and Rⁿ is
 a linear or branched chain alkyl group and q is 2, 3, 4
 or 5.

20 The invention provides a compound having the structure:



30 wherein X is CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S,
 where R is a methyl, ethyl or propyl group; wherein Y is
 -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-,
 where h and k are independently the same or different and
 35 are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-,
 where h and k are independently the same or different and
 are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR',

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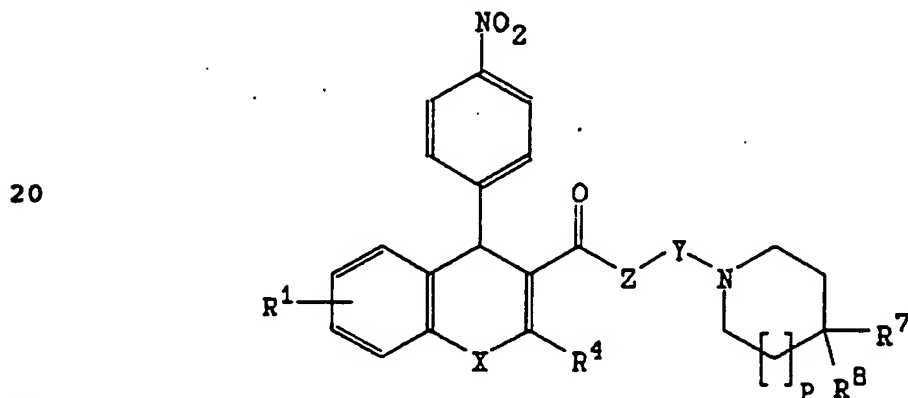
NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R¹ is H, Cl, Br, I, F, NO₂, CN, OH, OR''², OCOR''², NH₂, NR''², NHCOR''², or CF₃, where R''² is a linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, a linear, cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, N₃ or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)₄OH or COO(CH₂)₄OR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,

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furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v ,
 OCONHR^v , NH_2 , NHR^v , NR^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where
 R^v is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group and q is 2, 3, 4
 or 5. In one embodiment, the invention provides a
 15 compound having the structure:

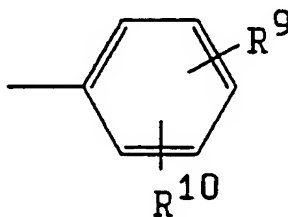


wherein X is CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S,
 where R is a methyl, ethyl or propyl group; wherein Y is
 $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$,
 where h and k are independently the same or different and
 30 are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$,
 where h and k are independently the same or different and
 are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR',
 NOR' or CH_2 , where R' is a methyl, ethyl or propyl group;
 wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R^1 is
 35 H, Cl, Br, I, F, NO_2 , CN, OH, OR''^2 , OCOR''^2 , NH_2 , NR''^2 ,
 NHCOR''^2 , or CF_3 , where R''^2 is a linear or branched chain
 alkyl group, or an aryl group; wherein R^4 is H, a linear,

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cyclic or branched chain alkyl, an alkoxyalkyl, azido-alkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2 W^0 (CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_q OH$ or $COO(CH_2)_q OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

25

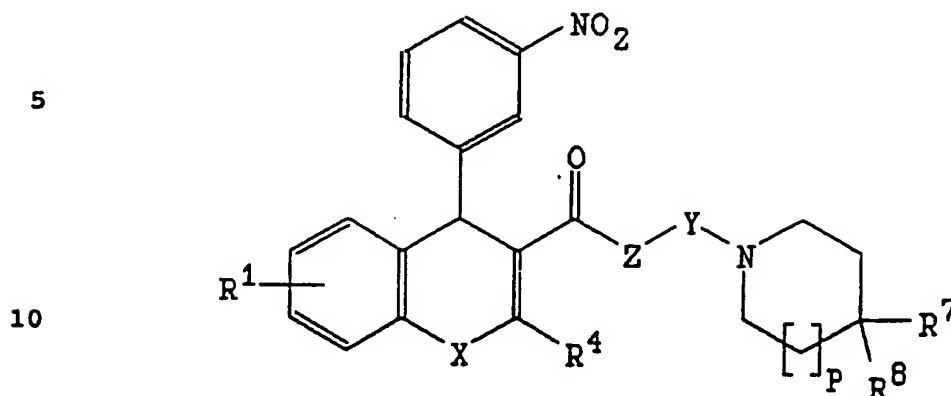


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group and q is 2, 3, 4

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or 5. In another embodiment, the invention provides a compound having the structure:



wherein X is CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein Y is

15 -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR',

20 NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R¹ is H, Cl, Br, I, F, NO₂, CN, OH, OR'', OCOR'', NH₂, NR'', NHCOR'' or CF₃, where R'' is a linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, a linear,

25 cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_jW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched

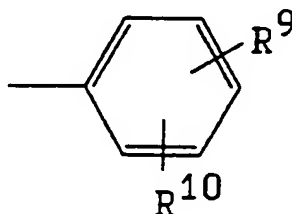
30 chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched

35 chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are

-30-

independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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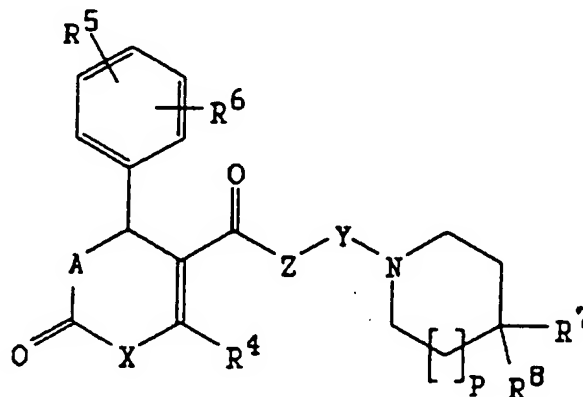


15 wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v, OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4
20 or 5.

The invention also provides a compound having the structure:

25

30



wherein A and X are independently the same or different
35 and are CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_n-O-(CH₂)₁-,

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where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR',

5 NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R⁴ is H, a linear, cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-

10 alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_jW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_jW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl

15 group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁵ and

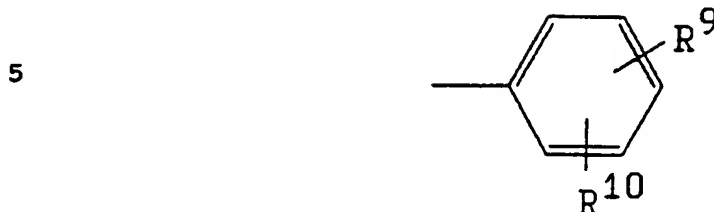
20 R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, N₃ or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone, or mono- or dialkylamino group, or together constitute a methylenedioxy group;

25 wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)₄OH or COO(CH₂)₄OR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl

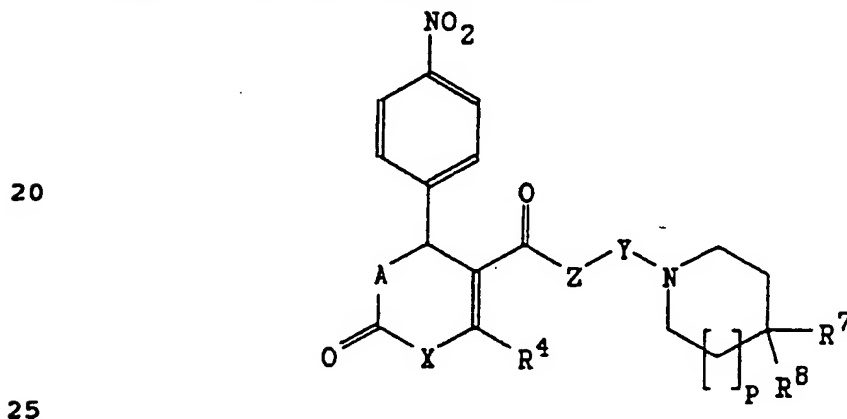
30 group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol,

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furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^n , OCOR^n , OCOOR^n ,
 OCONHR^n , NH_2 , NHR^n , NR^n , NHCOR^n , NHCOOR^n or NHCONHR^n , where
 R' is a linear or branched chain alkyl group, and R^n is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5. In one embodiment, the invention provides a
 15 compound having the structure:

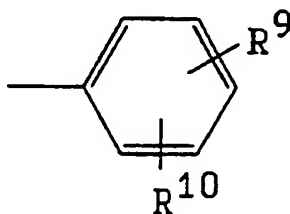


wherein A and X are independently the same or different
 and are CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S, where
 R is a methyl, ethyl or propyl group; wherein Y is -
 $(\text{CH}_2)_n$ -, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h\text{-O-}(\text{CH}_2)_k$ -,
 30 where h and k are independently the same or different and
 are 2, 3 or 4; $-(\text{CH}_2)_h\text{-CH=CH-}(\text{CH}_2)_k$ -, or $-(\text{CH}_2)_h\text{-C}\equiv\text{C-}(\text{CH}_2)_k$ -,
 where h and k are independently the same or different and
 are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR' ,
 NOR' or CH_2 , where R' is a methyl, ethyl or propyl group;
 35 wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R^4 is
 H, a linear, cyclic or branched chain alkyl, an
 alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-

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alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2 W^0 (CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or
 5 an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^-
 10 is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$,
 15 $COO(CH_2)_q OH$ or $COO(CH_2)_q OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

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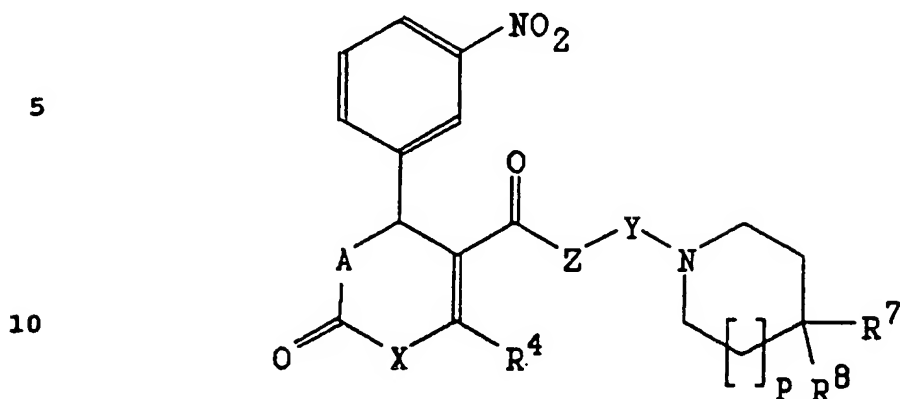


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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is
 30 a linear or branched chain alkyl group, and q is 2, 3, 4

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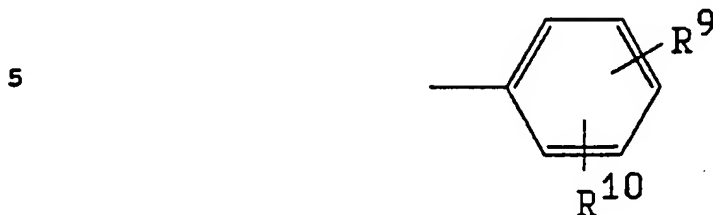
or 5. In another embodiment, the invention provides a compound having the structure:



wherein A and X are independently the same or different and are CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where
 15 R is a methyl, ethyl or propyl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and
 20 are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R^4 is H , or a linear or branched chain, or cyclic alkyl group; and wherein R^7 and R^8 are independently the same or
 25 different and are H , CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_4\text{OH}$ or $\text{COO}(\text{CH}_2)_4\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl,
 30 indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,

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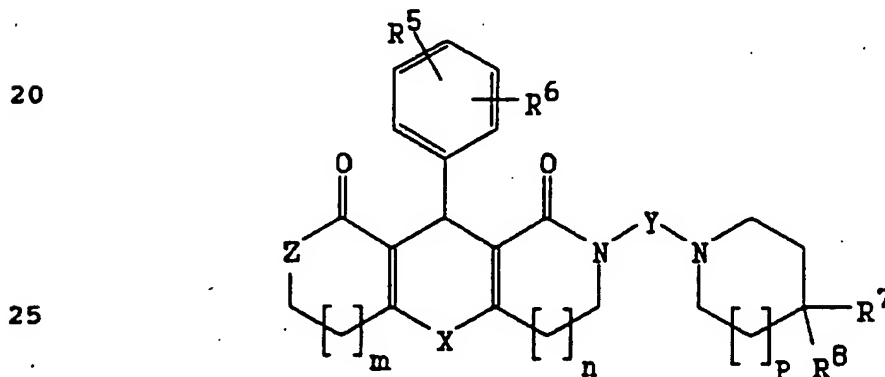
furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v ,
 OCONHR^v , NH_2 , NHR^v , NR^v_2 , NHCOR^v , NHCOOR^v or NHCONHR^v , where
 R^v is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5.

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The invention further provides a compound having the structure:

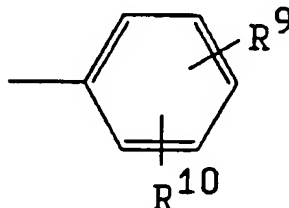


wherein X is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S ,
 where R is a methyl, ethyl or propyl group; wherein Y is
 30 $-(\text{CH}_2)_h-$, where h is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$,
 where h and k are independently the same or different and
 are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$,
 where h and k are independently the same or different and
 are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' ,
 35 NOR' or CH_2 , where R' is a methyl, ethyl or propyl group;
 wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein m
 and n are independently the same or different and are 0

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or 1; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , N_3 or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfone, or mono-
 5 or dialkylamino group, or together constitute a methylenedioxy group; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or
 10 $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

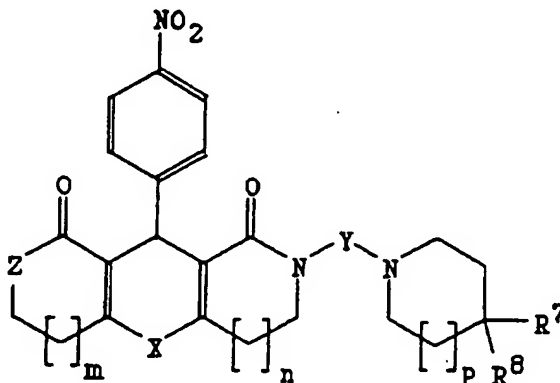
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR^v_2 , NHCOR^v , NHCOOR^v or NHCONHR^v , where R' is a linear or branched chain alkyl group, and R^v is
 25 a linear or branched chain alkyl group, and q is 2, 3, 4 or 5. In one embodiment, the invention provides a compound having the structure:

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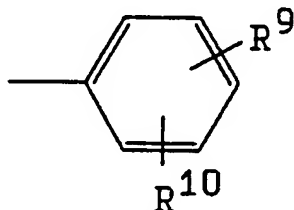


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wherein X is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein Y is $-(\text{CH}_2)_h-$, where h is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein m and n are independently the same or different and are 0 or 1; and wherein R^7 and R^8 are independently the same or different and are H , CN , CF_3 , OH , OR''' , OCOR''' , NH_2 , NHR''' , NR'''_2 , or NHCOR''' , where R''' is a linear chain alkyl group, a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

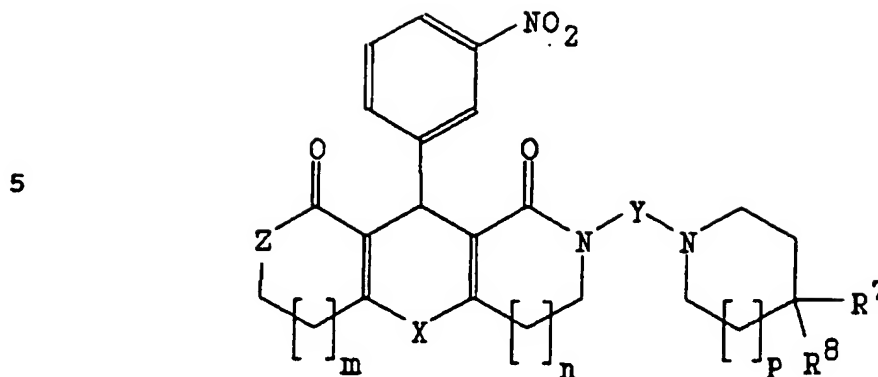
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25 wherein R^9 and R^{10} are independently the same or different and are H , Cl , Br , F , OH , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR^v_2 , NHCOR^v , NHCOOR^v or NHCONHR^v , where R^v is a linear or branched chain alkyl group. In another embodiment, the invention provides a compound having the

30 structure:

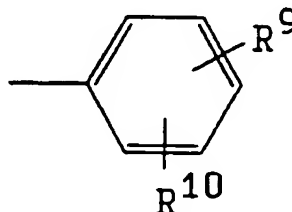
-38-



wherein X is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein Y is $-(\text{CH}_2)_h-$, where h is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$ where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein m, n, and p are independently the same or different and are 0 or 1; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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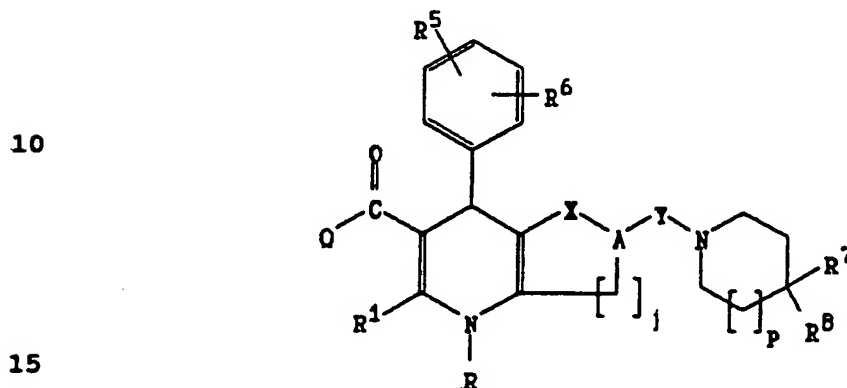


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where

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R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

- 5 The invention further provides a compound having the structure:

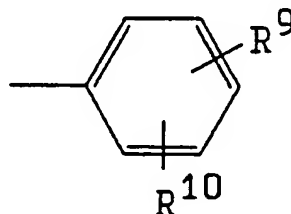


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂''', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4,

-40-

5 or 6; wherein X is C=O, CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R' is a methyl, ethyl or propyl group; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, N₃ or CF₃, or a
 5 linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone, or mono- or dialkyl-amino group, or together constitute a methylenedioxy group; wherein A is CH; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are
 10 independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein j is 1 or 2; wherein p is 0, 1 or 2; and wherein R⁷ and R⁸ are independently the same or different
 15 and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl,
 20 indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

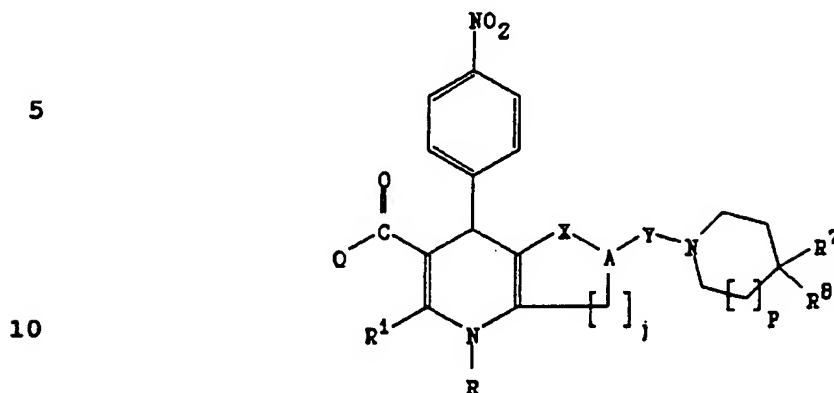
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wherein R⁹ and R¹⁰ are independently the same or different
 30 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v, OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4

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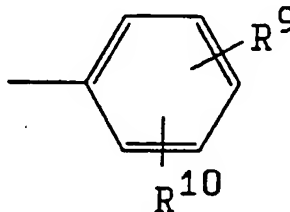
or 5. In one embodiment, the invention provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein X is C=O, CH₂, CR², NH, NR², NCHO, NCOR², NOH, O or S, where R² is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group; wherein A is CH; wherein Y is -(CH₂)_u-, where

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n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein j is 1 or 2; wherein p is 0, 1 or 2; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



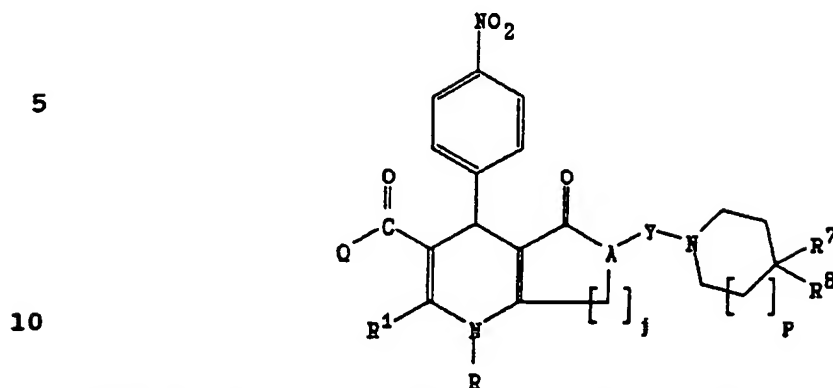
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4

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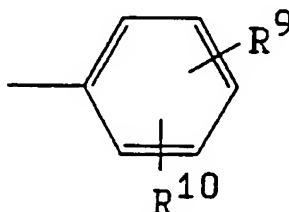
or 5. In another embodiment, the invention provides a compound having the structure:



wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR₂', NR''OH, NR''OR'' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein A is CH; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are

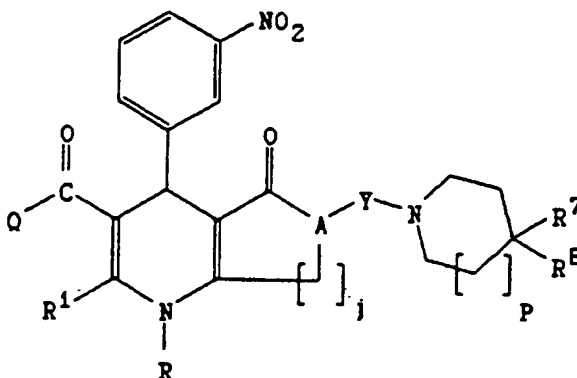
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1, 2, 3 or 4; wherein j is 1 or 2; wherein p is 0, 1 or 2; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $CONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5. In another embodiment, the invention provides a compound having the structure:



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wherein Q is OH, OR''' , SH, SR''' , NH_2 , NHR''' , NR'''_2 , $NR'''OH$, $NR'''OR'''$ or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R''' is H, a linear or

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branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)₁W, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z', NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)₁W¹,
 5 or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z', NHCOR', N₃ or NO₂, and
 10 where R' is a linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein A is CH; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are
 15 independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein j is 1 or 2; wherein p is 0, 1 or 2; and wherein R⁷ and R⁸ are independently the same or different
 20 and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)₄OH or COO(CH₂)₄OR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl,
 30 indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,

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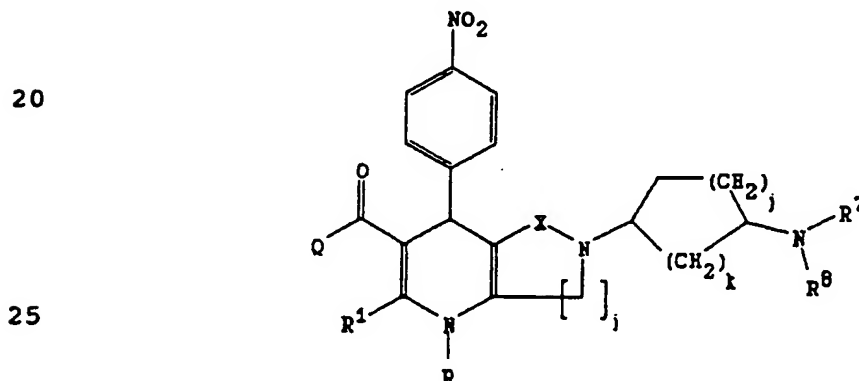
furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v ,
 OCONHR^v , NH_2 , NHR^v , NR^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where
 R^v is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5.

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The invention still further provides a compound having the structure:



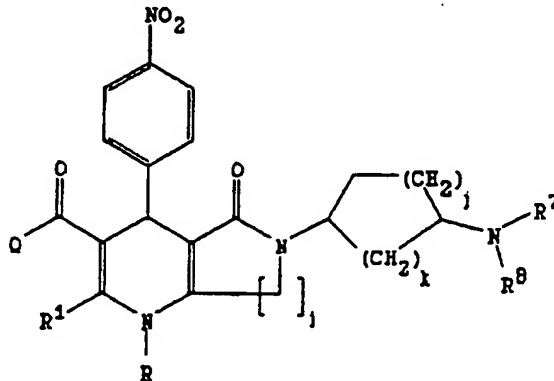
wherein X is C=O , CH_2 , CR^a , NH , NR^a , NCHO , NCOR^a , NOH , O or
 S , where R^a is a methyl, ethyl or propyl group; wherein Q
 is OH , OR'' , SH , SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}'''\text{OH}$,
 30 $\text{NR}'''\text{OR}'''$ or a linear or branched chain alkyl group, or
 an arylalkyl group, or an alkenyl or alkynyl group, or an
 aryl group, where R'' is H, a linear or branched chain
 alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl
 group, and R''' is a linear or branched chain alkyl
 35 group, or an aryl group; wherein R is H, a linear or
 branched chain alkyl or acyl group, or an aryl group;
 wherein R^1 is H, a linear or branched chain alkyl, an

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alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_iW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 , or $CH_2W^0(CH_2)_jW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein i is 1 or 2; and wherein j and k are independently the same or different and are 0, 1, 2 or 3. In one embodiment, the invention provides a compound having the structure:

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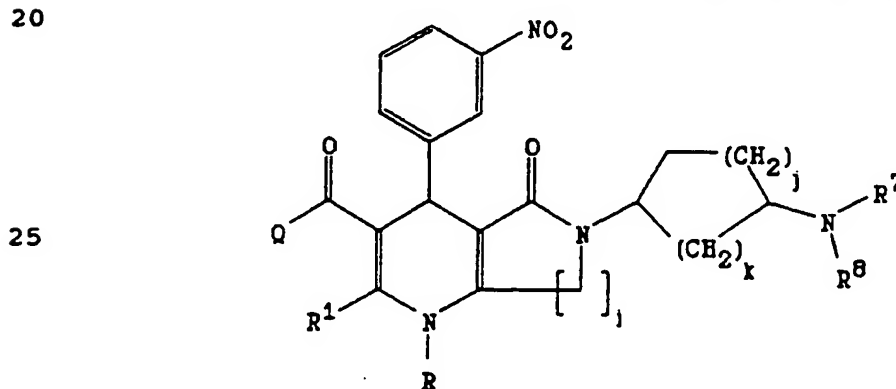


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR'''OH$, $NR'''OR'''$ or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^1 is H, a linear or branched chain

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alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_W$,
5 or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and
10 where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^j and R^i are independently the same or different and are a linear or branched chain alkyl group,
15 or an aryl group; wherein i is 1 or 2; and wherein j and k are independently the same or different and are 0, 1, 2 or 3.

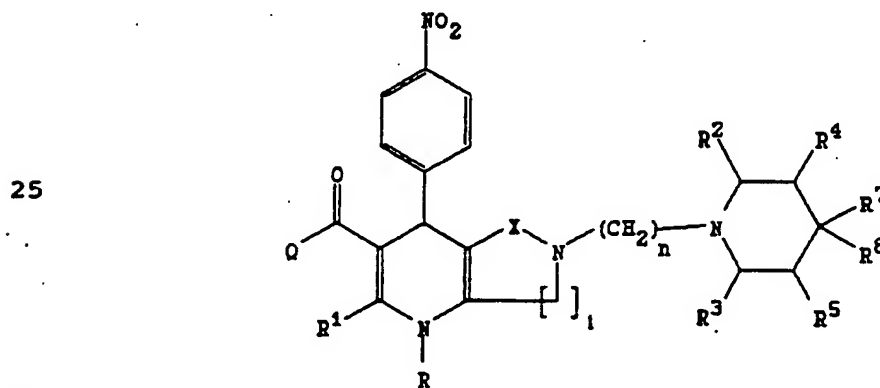
The invention provides a compound having the structure:



30 wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'',
NR''OH, NR''OR''' or a linear or branched chain alkyl
group, or an arylalkyl group, or an alkenyl or alkynyl
group, or an aryl group, where R'' is H, a linear or
35 branched chain alkyl group, trialkylsilylalkyl,
cyanoalkyl or an aryl group, and R''' is a linear or
branched chain alkyl group, or an aryl group; wherein R

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is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein i is 1 or 2; and wherein j and k are independently the same or different and are 0, 1, 2 or 3. In one embodiment, the invention provides a compound having the structure:



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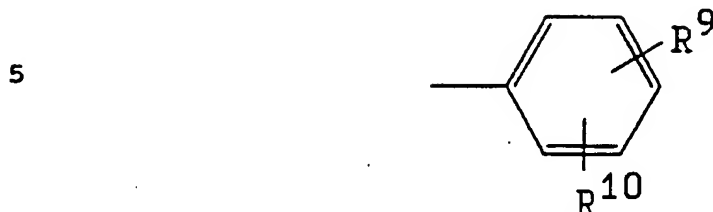
wherein X is $C=O$, CH_2 , CR^a , NH , NR^a , $NCHO$, $NCOR^a$, NOH , O or S , where R^a is a methyl, ethyl or propyl group; wherein Q is OH , OR'' , SH , SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$ or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl

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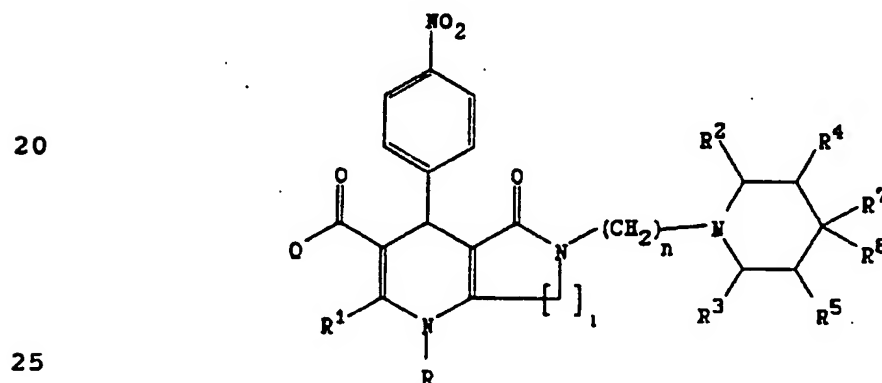
group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an
5 alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or
10 an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻
15 is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R² and R³ are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein R⁴ and R⁵ are independently the same or different
20 and are a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂',
25 NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl,

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furyl or thiophene group, or an aryl group having the structure:



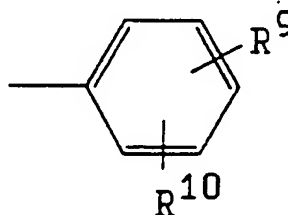
wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v ,
 OCONHR^v , NH_2 , NHR^v , NR^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where
 R' is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein i is 1 or 2; and wherein n is 2, 3 or 4.
 15 In another embodiment, the invention provides a compound
 having the structure:



wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' ,
 $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$ or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl
 30 group, or an aryl group, where R'' is H, a linear or
 branched chain alkyl group, trialkylsilylalkyl,
 cyanoalkyl or an aryl group, and R''' is a linear or
 branched chain alkyl group, or an aryl group; wherein R
 is H, a linear or branched chain alkyl or acyl group, or
 35 an aryl group; wherein R^1 is H, a linear or branched chain
 alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl,
 azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl,

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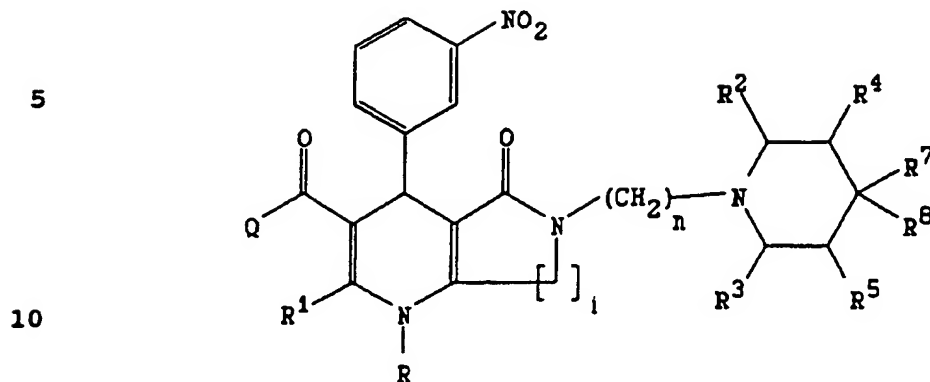
hydroxyalkyl or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 and R^3 are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein R^4 and R^5 are independently the same or different and are a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein i is 1 or 2; and wherein n is 2, 3 or 4.

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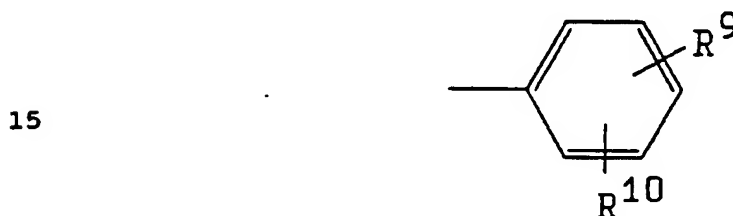
In another embodiment, the invention provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂''', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N*R',Z', NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N*R',Z', NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R² and R³ are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein R⁴ and R⁵ are independently the same or different and are a linear or branched chain

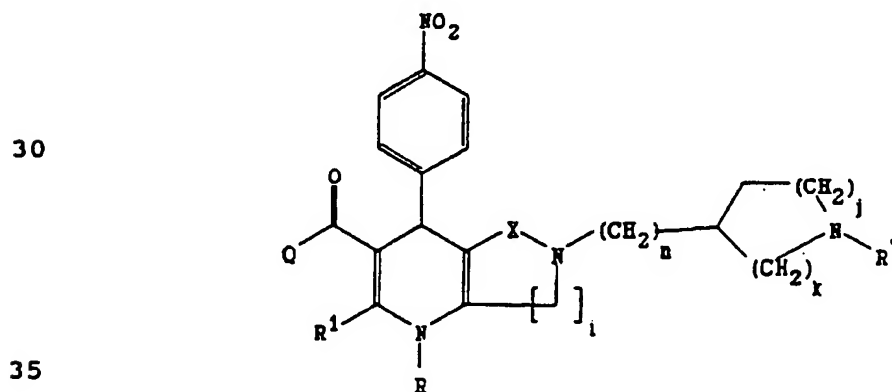
-54-

alkyl, alkoxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



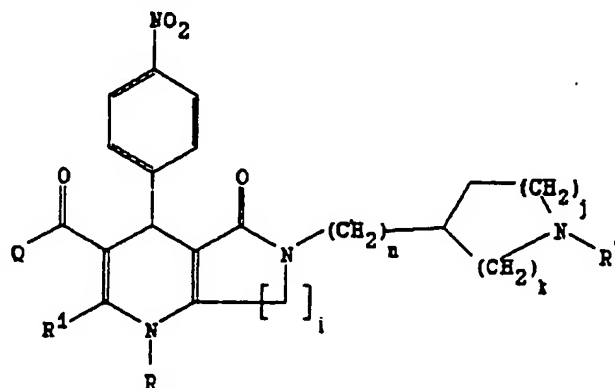
wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein i is 1 or 2; and wherein n is 2, 3 or 4.

25 The invention also provides a compound having the structure:



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wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ is an aryl or diarylalkyl group; wherein i is 1 or 2; wherein n is 2, 3 or 4; and wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4. In one embodiment, the invention provides a compound having the structure:

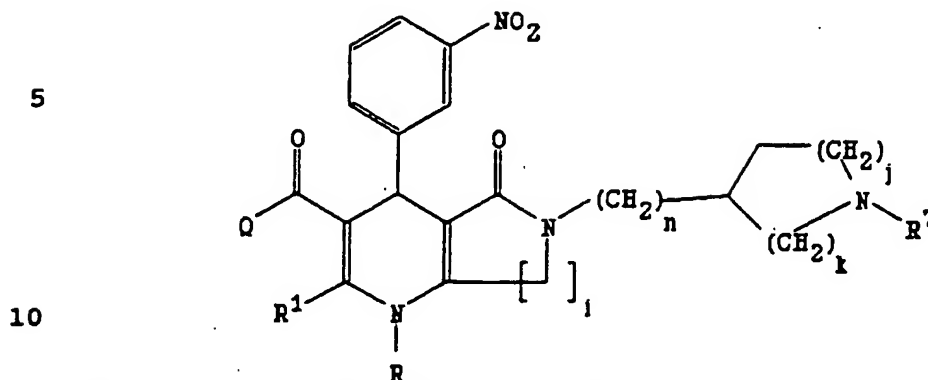


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wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ is an aryl or diarylalkyl group; wherein i is 1 or 2; wherein n is 2, 3 or 4; and wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4.

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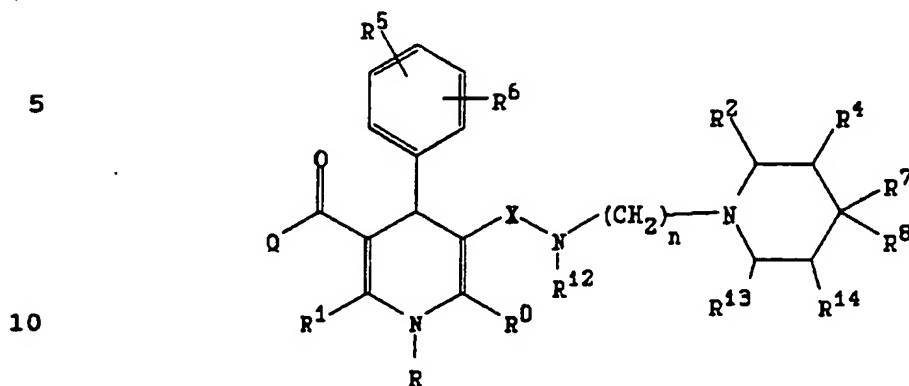
The invention further provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ is an aryl or diarylalkyl group; wherein i is 1 or 2; wherein n is 2, 3 or 4; and wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4.

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The invention further provides a compound having the structure:



wherein X is C=O, CH₂, CR₂, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Q

15 is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl

20 group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an

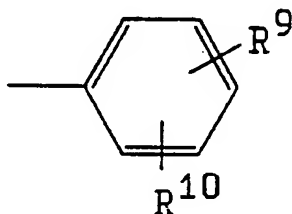
25 alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or

30 an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻

35 is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H, a linear or branched chain alkyl or acyl group, or an

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aryl group; wherein R^2 , R^3 , and R^4 are independently the same or different and are H, or a linear or branched chain alkyl, hydroxyalkyl, alkoxyalkyl, amino alkyl, or aryl group; wherein R^4 is a linear or branched chain alkyl, alkoxyalkyl, hydroxyalkyl, or a linear or branched chain alkenylalkyl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , N_3 , CF_3 , a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



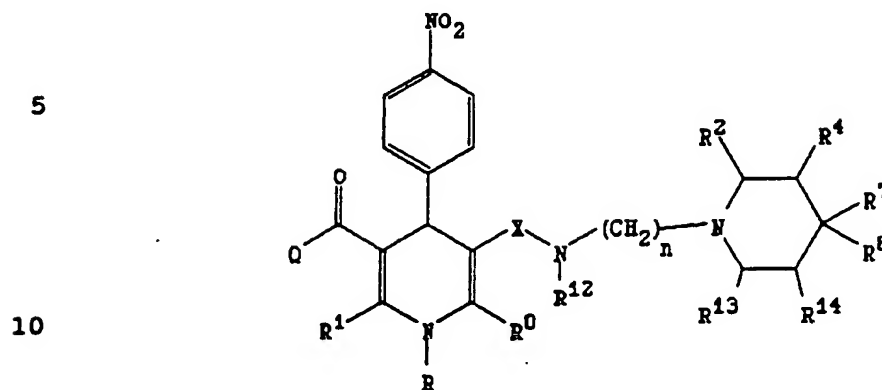
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$; where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and

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wherein n is 2, 3 or 4. In one embodiment, the invention provides a compound having the structure:



wherein X is C=O, CH₂, CR², NH, NR³, NCHO, NCOR⁴, NOH, O or S, where R³ is a methyl, ethyl or propyl group; wherein Q

15 is OH, OR⁵, SH, SR⁶, NH₂, NHR⁷, NR⁸, NR⁹OH, NR¹⁰OR¹¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R⁵ is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl

20 group, and R⁶ is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an

25 alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR¹², NR¹³, NHOH, N⁺R¹⁴Z⁻, NHCOR¹⁵, N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl

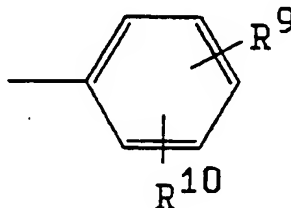
30 group, or an alkenyl or alkynyl group, or an aryl group, where R¹² is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR¹², NR¹³, NHOH, N⁺R¹⁴Z⁻, NHCOR¹⁵, N₃ or NO₂, and where R¹⁴ is a linear or branched chain alkyl group, or an aryl group,

35 where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H, a linear or branched chain alkyl or acyl group,

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or an aryl group; wherein R^2 , R^{13} , and R^{14} are independently the same or different and are H, or a linear or branched chain alkyl, hydroxyalkyl, alkoxyalkyl, amino alkyl, or aryl group; wherein R^4 is a linear or branched chain
 5 alkyl, alkoxyalkyl, hydroxyalkyl, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or
 10 $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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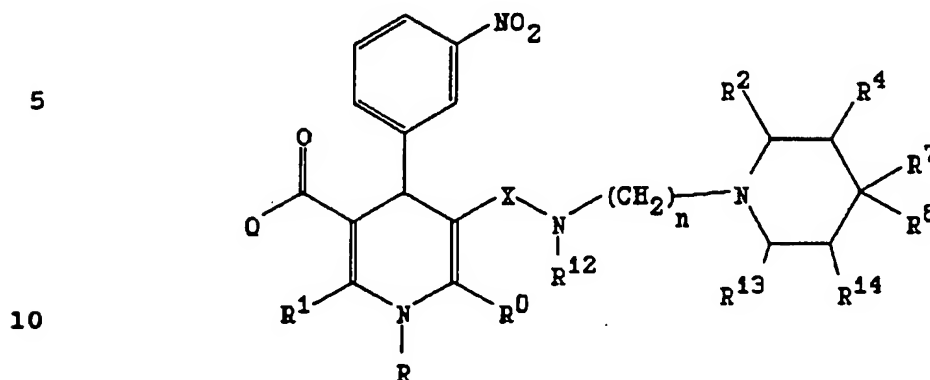


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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where
 25 R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and

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wherein n is 2, 3 or 4. In another embodiment, the invention provides a compound having the structure:



wherein X is C=O, CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Q

15 is OH, OR^{''}, SH, SR^{'''}, NH₂, NHR^{'''}, NR₂^{'''}, NR^{''}OH, NR^{''}OR^{'''}, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R^{''} is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl

20 group, and R^{'''} is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an

25 alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR['], NR₂['], NHOH, N⁺R₃'Z⁻, NHCOR['], N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl

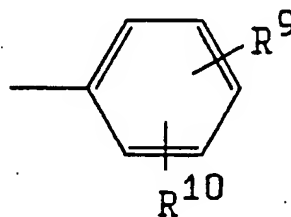
30 group, or an alkenyl or alkynyl group, or an aryl group, where R['] is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR['], NR₂['], NHOH, N⁺R₃'Z⁻, NHCOR['], N₃ or NO₂, and where R['] is a linear or branched chain alkyl group, or an aryl group,

35 where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R², R¹³, and R¹⁴ are independently the same or different and

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are H, or a linear or branched chain alkyl, hydroxyalkyl, alkoxyalkyl, amino alkyl or aryl group; wherein R^4 is a linear or branched chain alkyl, alkoxyalkyl, hydroxyalkyl, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

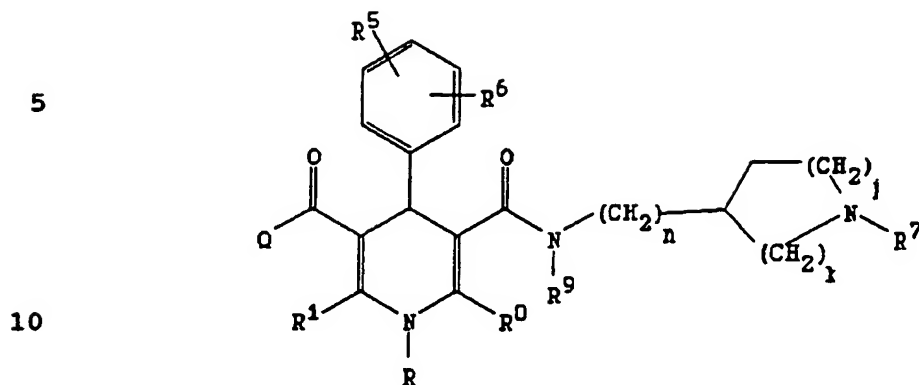
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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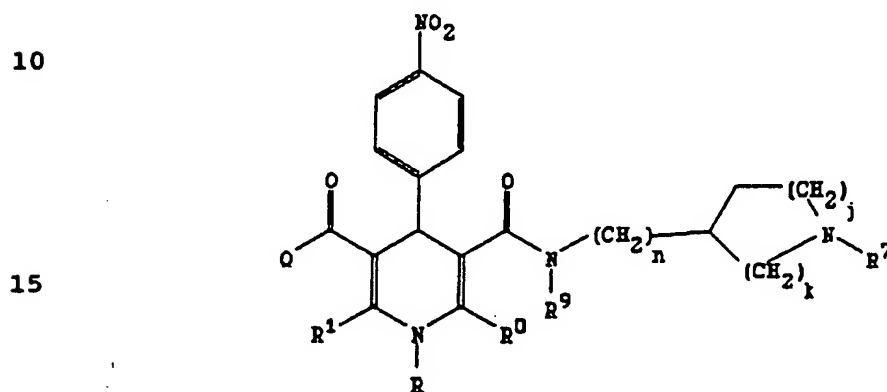
The invention also provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, N₃, CF₃, a linear or branched chain alkyl, alkoxy, alkoxy-

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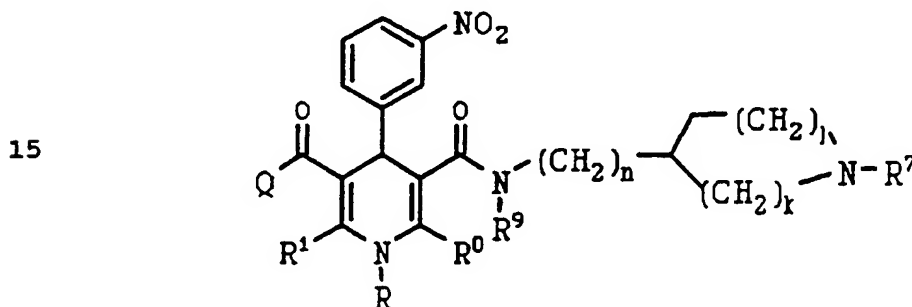
carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^7 is an aryl or diarylalkyl group; wherein R^9 is H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2 or 3; and wherein n is 2, 3 or 4. In one embodiment, the invention provides a compound having the structure:



wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_nW, where W is NH₂, NHR', NR', NHOH, N⁺R'₃Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_mW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR', NHOH, N⁺R'₃Z⁻, NHCOR', N₃ or NO₂, and

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where R' is a linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁷ is an aryl or diarylalkyl group; wherein R⁹ is a H or linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2 or 3; and wherein n is 2, 3 or 4. In another embodiment, the invention provides a compound having the structure:



20 wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂''', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N'R₃'Z', NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl

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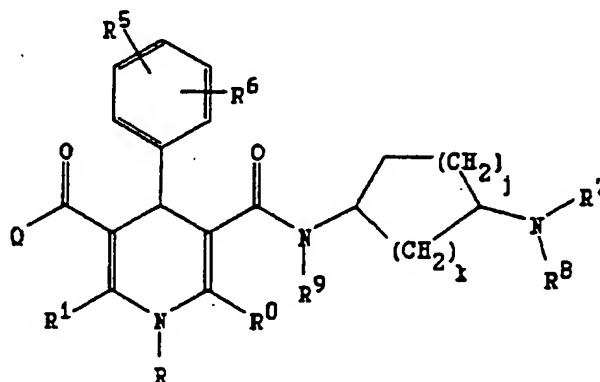
-67-

group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R' is an aryl or diarylalkyl group; wherein R^0 is H or a linear chain alkyl group; and wherein j and k are independently the same or different and are 0, 1, 2 or 3.

The invention provides a compound having the structure:

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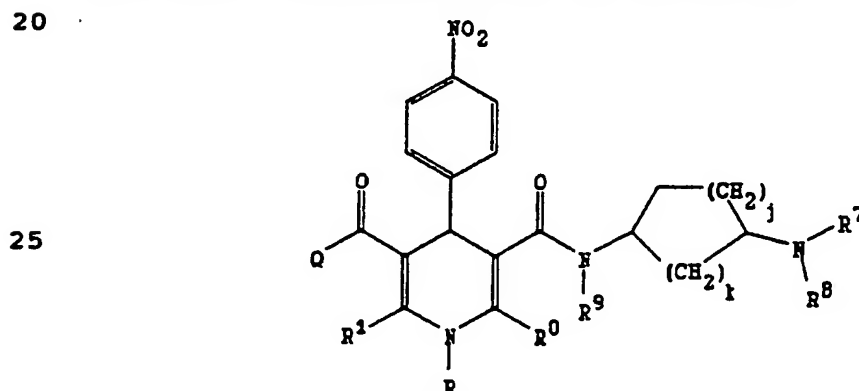
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25 wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR'''OH$, $NR'''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_jW$, where W is NH_2 ,

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NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, N₃, CF₃, a linear or branched chain alkyl, alkoxy, alkoxy-carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R⁷ is an aryl or diarylalkyl group; wherein R⁹ is a linear chain alkyl group; and wherein j and k are independently the same or different and are 0, 1, 2 or 3. In one embodiment, the invention provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the

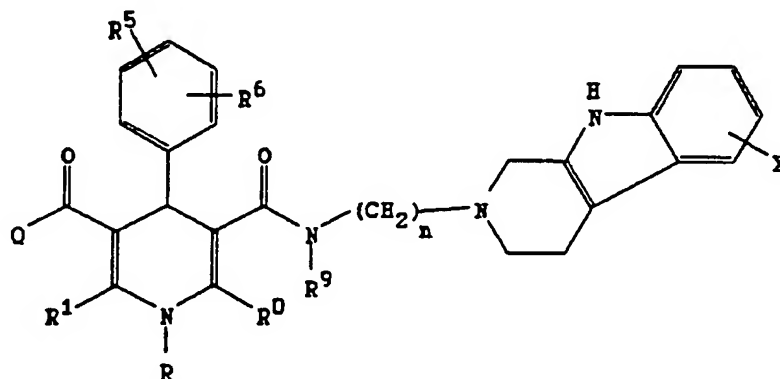
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same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^0 is a linear chain alkyl group; and wherein j and k are independently the same or different and are 0, 1, 2 or 3.

The invention also provides a compound having the structure:

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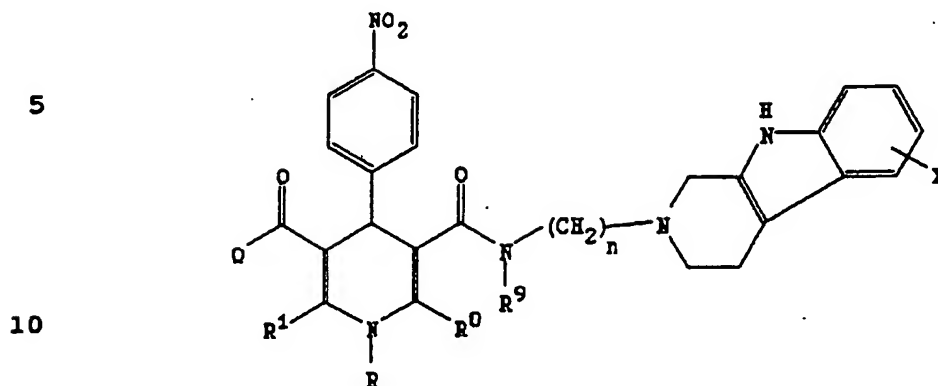
wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR'''OH$, $NR'''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the

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same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 ,
5 NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$,
or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1
10 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and
where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4,
5 or 6; wherein X is H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , or
15 CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different
20 and are H, or a linear or branched chain alkyl, alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, or hydroxylalkyl group, or an aryl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F,
25 NO_2 , N_3 , CN, NH_2 , or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^9 is H or a linear chain alkyl group; and wherein n is 2, 3 or

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4. In one embodiment, the invention provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R

20 is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl,

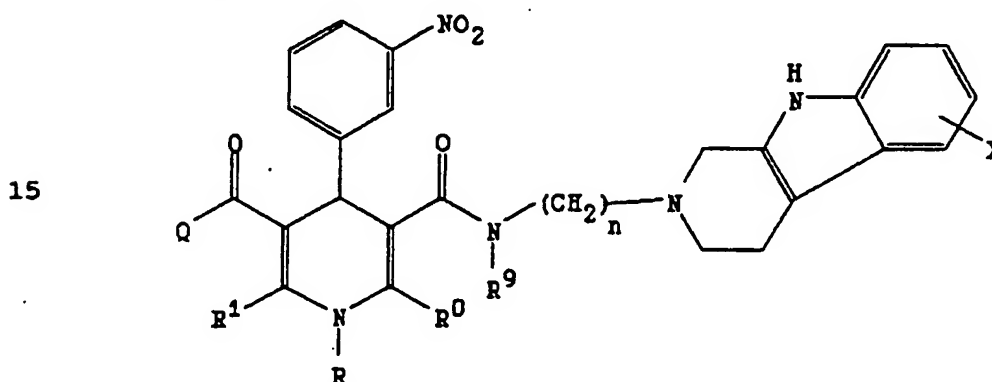
25 hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R'₃Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl

30 group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R'₃Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4,

35 5 or 6; wherein X is H, OH, Cl, Br, I, F, NO₂, CN, NH₂, or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or

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mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, or a linear or branched chain alkyl, alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, or hydroxylalkyl group, or an aryl group; wherein R⁹ is H or a linear chain alkyl group; and wherein n is 2, 3 or 4. In another embodiment, the invention provides a compound having the structure:

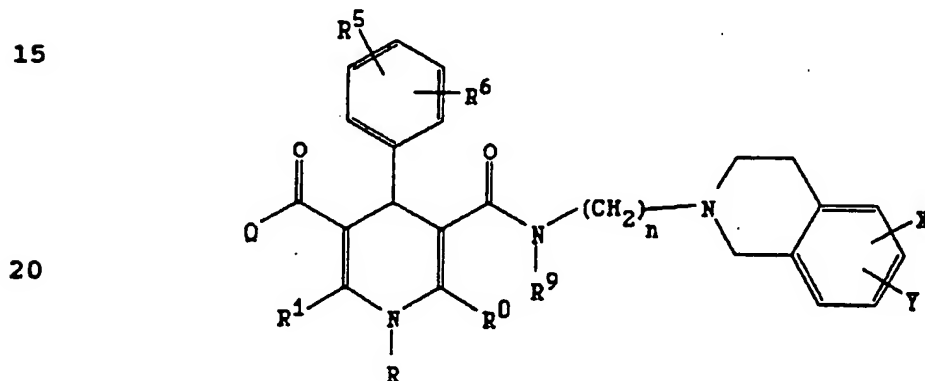


20 wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein X is H, OH, Cl, Br, I, F, NO₂, CN, NH₂, or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_nW, where W is NH₂, NHR',

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NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^9 is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

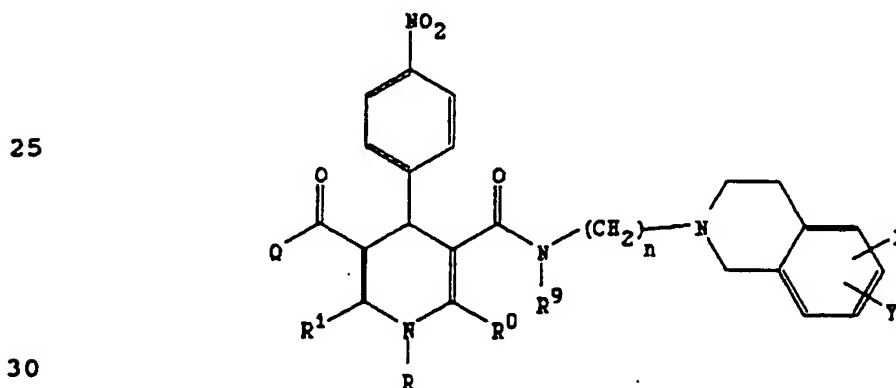
The invention provides a compound having the structure:



wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}'''\text{OH}$, $\text{NR}'''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein X and Y are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear

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or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 , or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , N_3 , CN, NH_2 , or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^9 is H or a linear chain alkyl group; and wherein n is 2, 3 or 4. In one embodiment, the invention provides a compound having the structure:



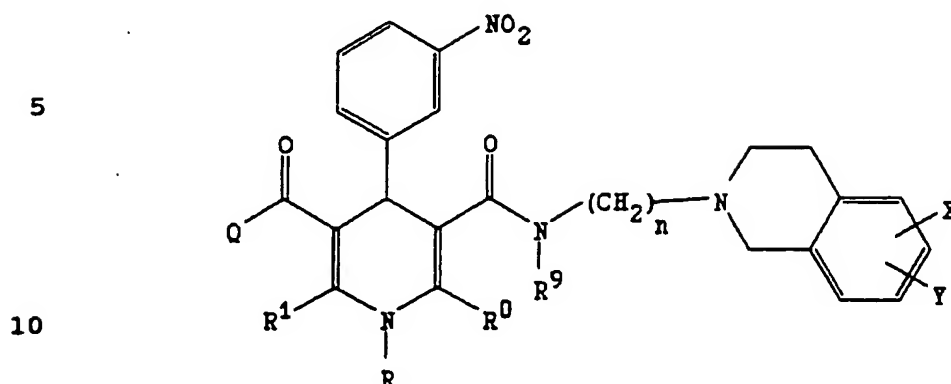
wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein X

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and Y are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein X and Y are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R⁹ is H or a linear chain alkyl group; and wherein n is 2, 3 or 4. In

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another embodiment, the invention provides a compound having the structure:

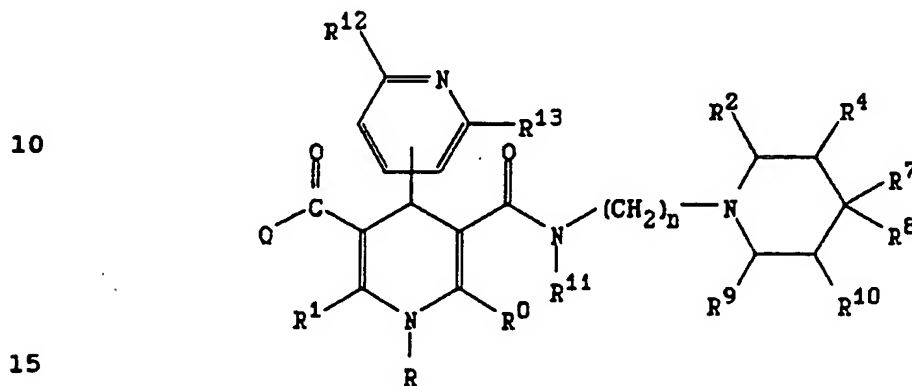


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein X and Y are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_nW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z', NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_mW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z', NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically

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acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^9 is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

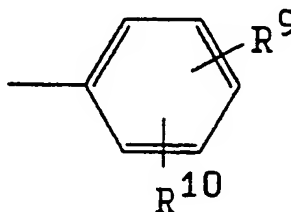
- 5 The invention further provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a

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linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is a H or linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



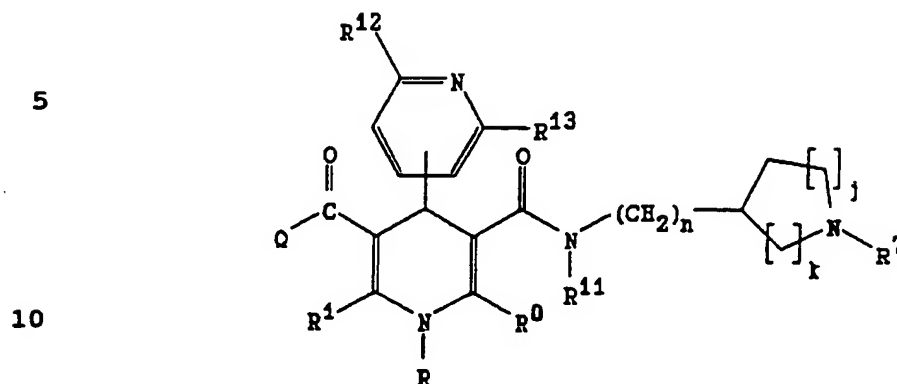
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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The invention still further provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R

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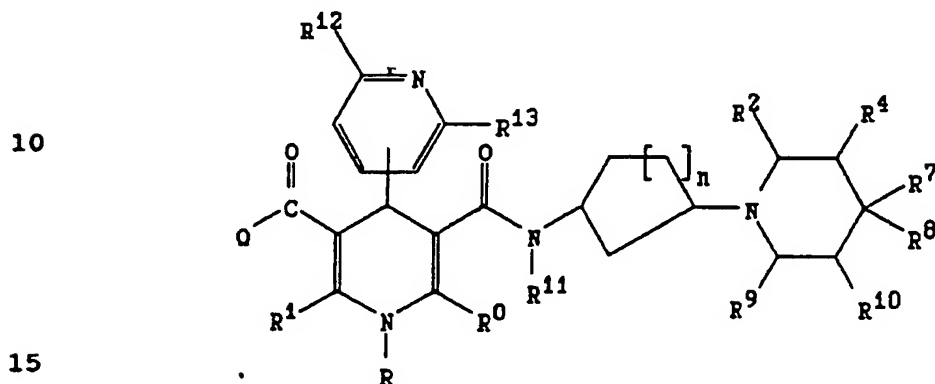
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is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ is an aryl or diarylalkyl group; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² and R¹³ are independently the same or different and are H

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or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

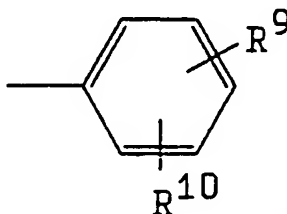
5 The invention also provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_nW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_nW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable

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counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

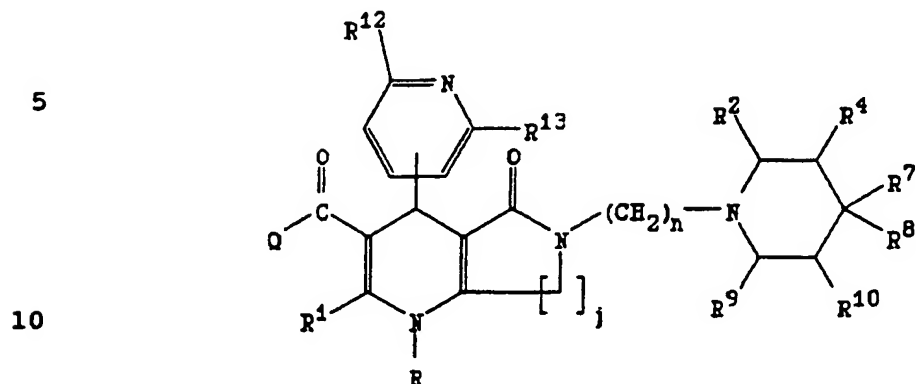


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 0, 1, 2, 3 or 4.

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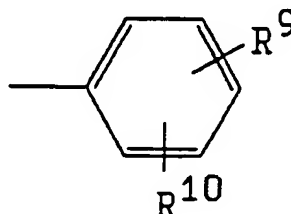
In addition, the invention provides a compound having the structure:



wherein Q is OH , OR'' , SH , SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H , a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^1 is H , a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O , S or NH , where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 , R^9 and R^{10} are independently the same or different and are a linear or branched chain alkyl group; wherein R^4 is a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a

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hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$,
 5 $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 10 group, or an aryl group having the structure:



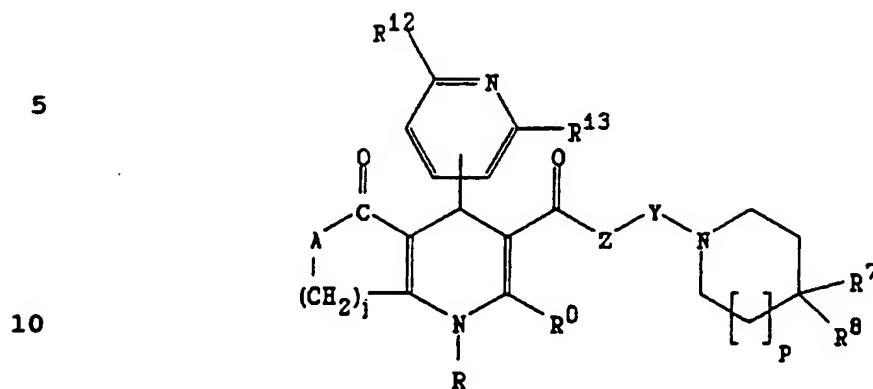
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where
 20 R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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The invention also provides a compound having the structure:

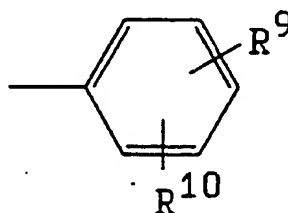


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH₂, CR₂, NH, NR', NCHO, NCOR', NOH, O or S, where R' is a methyl, ethyl or propyl group; wherein Z is O, NH, NCHO, NCOR', NR', NOR', or CH₂, where R' is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_W, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z', NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_W¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹

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is NH_2 , NHR' , NR'_2 , NHOH , $\text{N}^+\text{R}'_3\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are H , CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

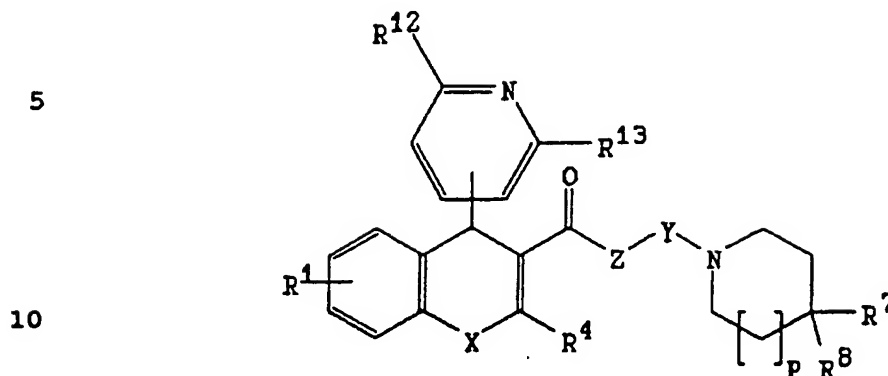
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20 wherein R^9 and R^{10} are independently the same or different and are H , Cl , Br , I , F , OH , NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

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The invention further provides a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-$, $O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^1 is H, Cl, Br, I, F, NO_2 , CN, OH, OR^2 , $OCOR^2$, NH_2 , NR^2 , $NHCOR^2$, or CF_3 , where R^2 is a linear or branched chain alkyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO, COR' , COSH, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,

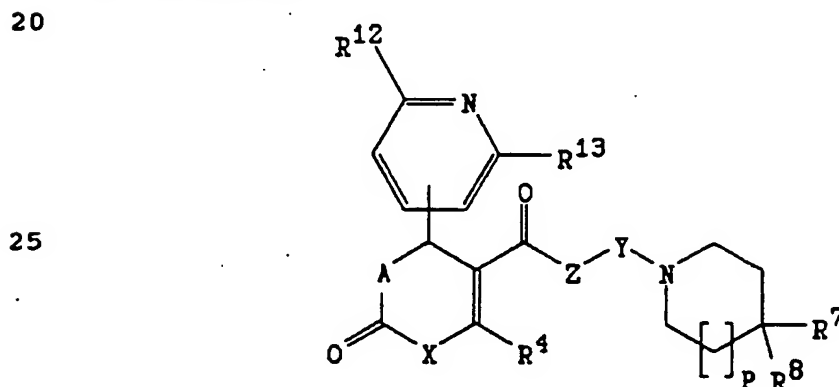
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quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR^v_2 , NHCOR^v , NHCOOR^v or NHCONHR^v , where R^v is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or
 15 different and are H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

The invention still further provides a compound having the structure:

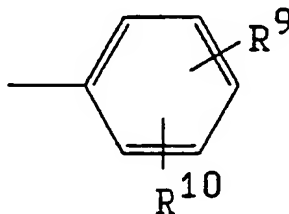


wherein A is CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S,
 30 where R is a methyl, ethyl or propyl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}=\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and
 35 are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein X is NH, NR'' , O or S, where R'' is H or a linear

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or branched chain alkyl or acyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' ,
 5 $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$,
 $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or
 $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,
 10 quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:

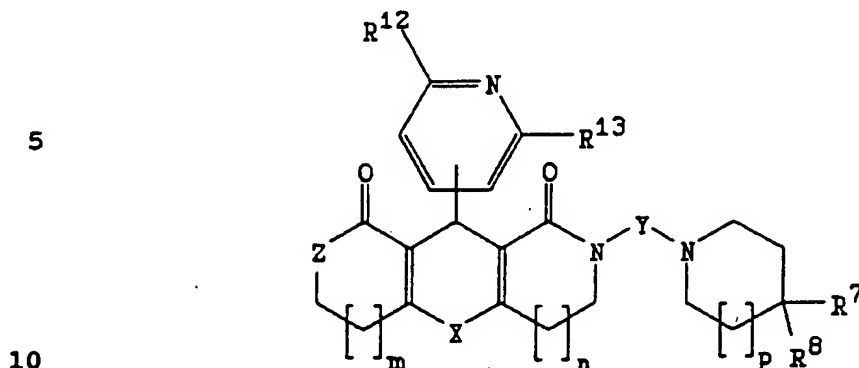
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$,
 20 $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where
 R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and
 25 wherein p is 0, 1, 2 or 3.

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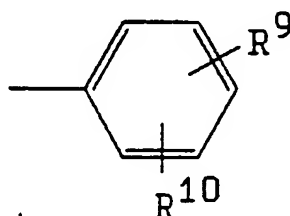
The invention provides a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_k-O-(CH_2)_h-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein X is NH, NR' , O, or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_4OH$ or $COO(CH_2)_4OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

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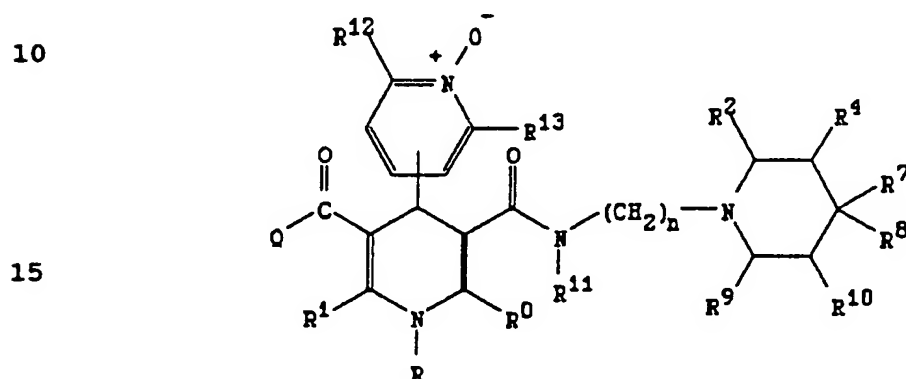
wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is

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a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

The invention also provides a compound having the structure:

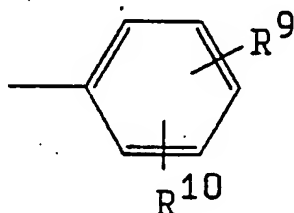


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'',
 20 NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or
 25 branched chain alkyl group, or an aryl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl,
 30 hydroxyalkyl, or an aryl group, or (CH₂)_pW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_pW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an
 35 aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and

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where R' is a linear or branched chain alkyl group, or an aryl group, where Z is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

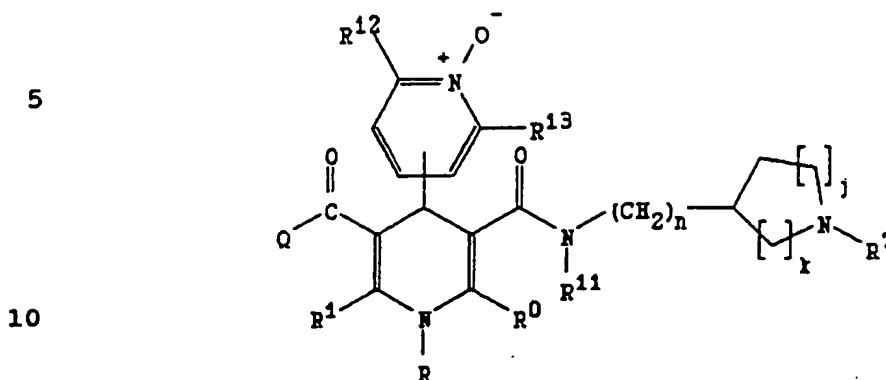
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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The invention further provides a compound having the structure:

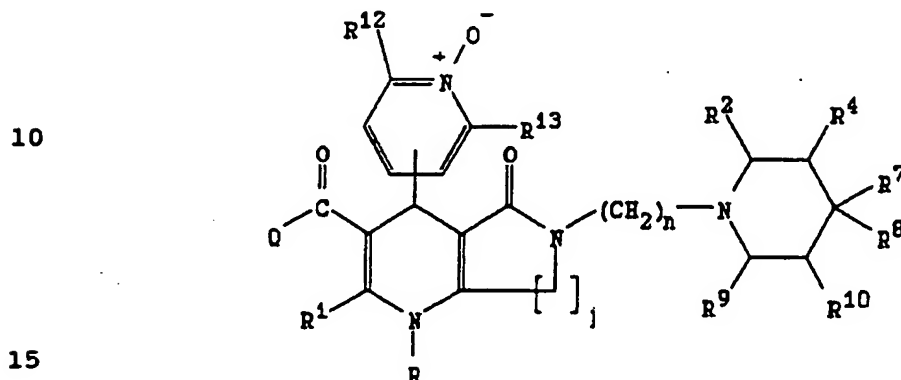


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁷ is an aryl or diarylalkyl group; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² and R¹³ are independently the same or different and are H or a

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linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

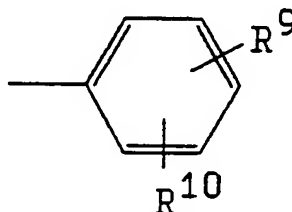
- 5 The invention still further provides a compound having the structure:



wherein Q is OH , OR'' , SH , SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H , a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R' is H , a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O , S or NH , where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl

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group; wherein R^1 , R^9 and R^{10} are independently the same or different and are a linear or branched chain alkyl group; wherein R^4 is a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:



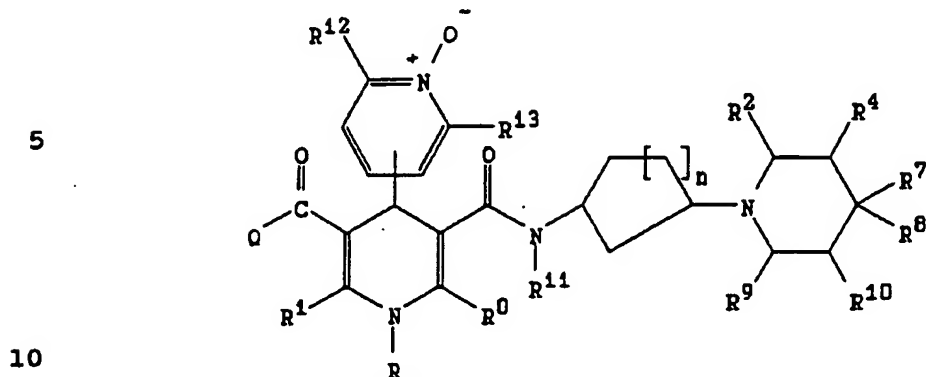
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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The invention provides a compound having the structure:

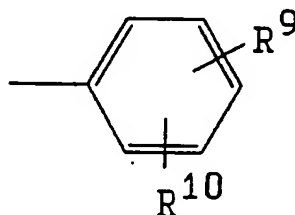


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group;

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wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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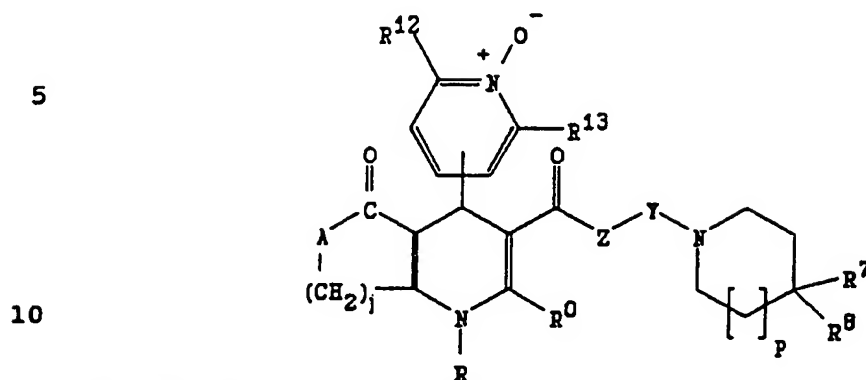
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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The invention also provides a compound having the structure:



wherein R^0 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2 W^0 (CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH_2 , CR^a_2 , NH, NR^a , $NCHO$, $NCOR^a$, NOH , O or S, where R^a is a methyl, ethyl or propyl group; wherein Z is O, NH, $NCHO$, $NCOR^a$, NR^a , NOR^a , or CH_2 , where R^a is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_q OH$ or

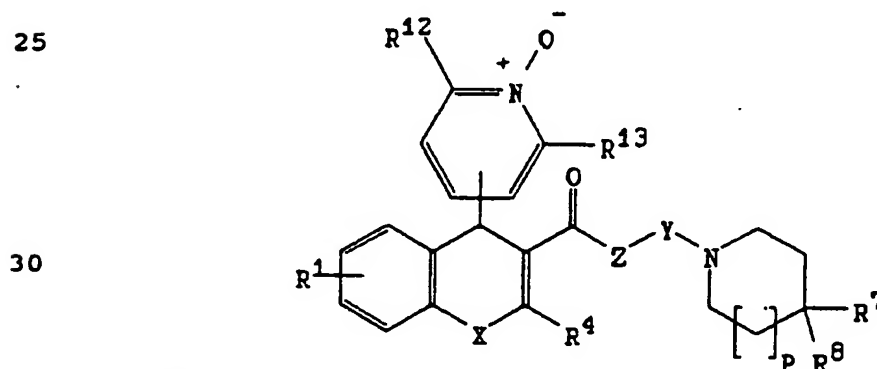
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COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, ORⁿ, OCORⁿ, OCOORⁿ, OCONHRⁿ, NH₂, NHRⁿ, NRⁿ, NHCORⁿ, NHCOORⁿ or NHCONHRⁿ, where
 15 R' is a linear or branched chain alkyl group, and Rⁿ is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² and R¹³ are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and
 20 wherein p is 0, 1, 2 or 3.

The invention further provides a compound having the structure:

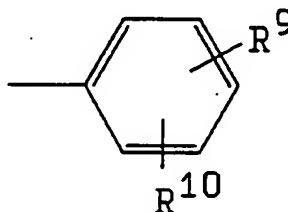


wherein X is NH, NR'', O, or S, where R'' is H or a linear or branched chain alkyl or acyl group, or an aryl group;
 35 group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -

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$(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; or an aryl group; wherein R^1 is H, Cl, Br, I, F, NO_2 , CN, OH, OR^2 , $OCOR^2$, NH_2 , NR^2 , $NHCOR^2$, or CF_3 , where R^2 is a linear or branched chain alkyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

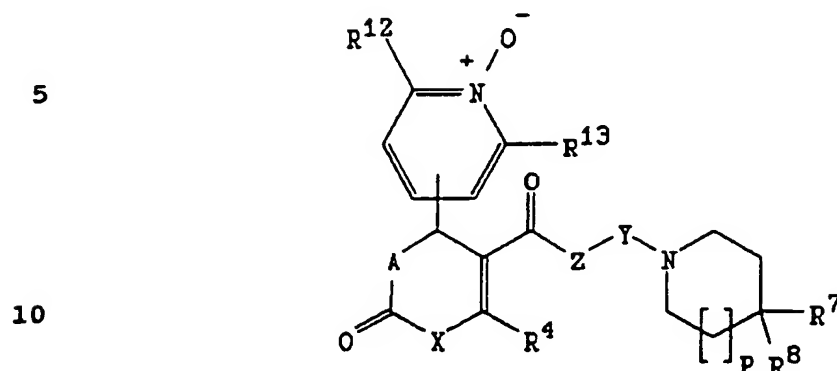
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $CONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

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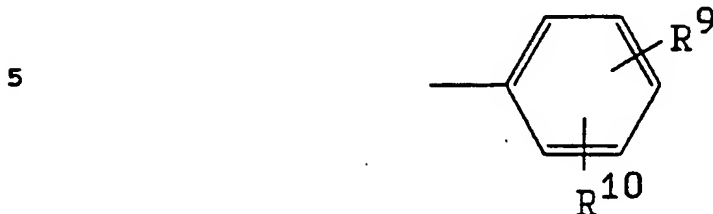
The invention still further provides a compound having the structure:



wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein X is NH , NR'' , O , or S , where R'' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R' is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_4\text{OH}$ or $\text{COO}(\text{CH}_2)_4\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,

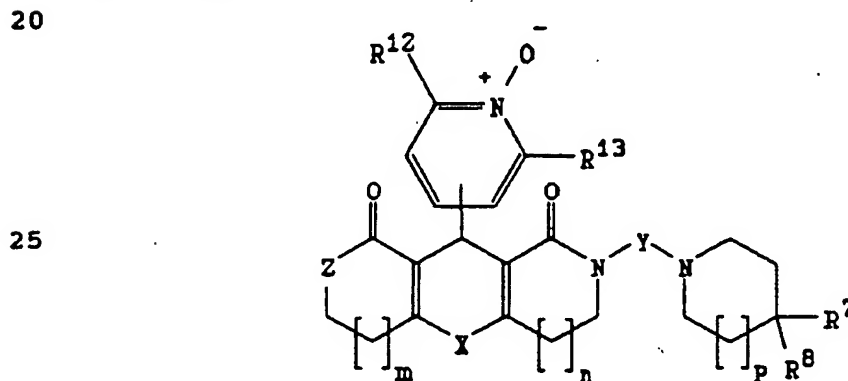
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quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v ,
 OCONHR^v , NH_2 , NHR^v , NR_2^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where
 R^v is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R^{12} and R^{13} are independently the same or
 15 different and are H or a linear chain alkyl group; and
 wherein p is 0, 1, 2 or 3.

The invention also provides a compound having the
 structure:

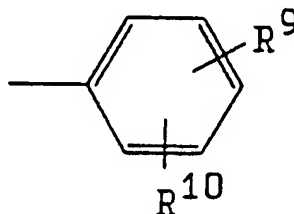


wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-$
 30 $\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or
 different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or
 $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the
 same or different and are 1, 2, 3 or 4; wherein Z is O,
 NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl
 35 or propyl group; wherein X is NH, NR' , O, or S, where R'
 is H or a linear or branched chain alkyl or acyl group,
 or an aryl group; wherein R^7 and R^8 are independently the

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same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

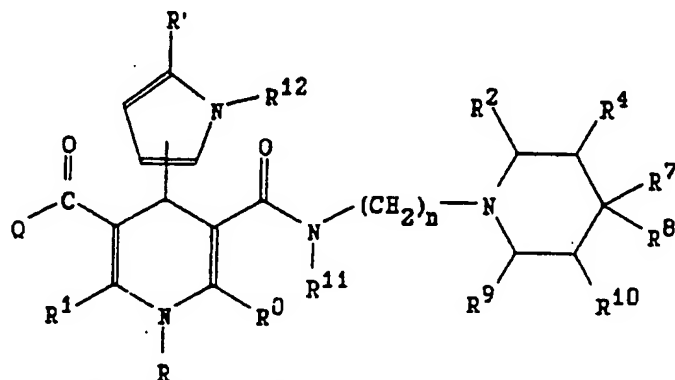
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15 wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, ORⁿ, OCORⁿ, OCOORⁿ, OCONHRⁿ, NH₂, NHRⁿ, NRⁿ₂, NHCORⁿ, NHCOORⁿ or NHCONHRⁿ, where R' is a linear or branched chain alkyl group, and Rⁿ is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² and R¹³ are independently the same or different and are H or a linear chain alkyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

25 The invention further provides a compound having the structure:

30



35

wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR''₂, NR''OH, NR''OR'', or a linear or branched chain alkyl

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group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or

5 branched chain alkyl group, or an aryl group; wherein R^0 , R^1 and R' are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl

10 group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0

15 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a

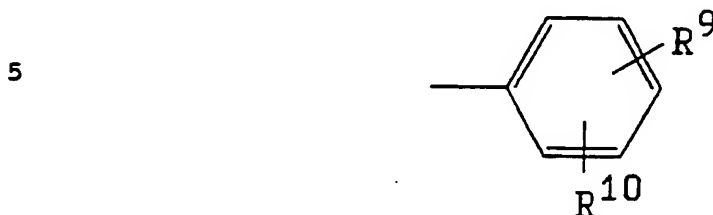
20 linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a

25 hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR', OCOR', NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, COOH, COOR', CHO, COR', COSH, COSR', $COO(CH_2)_q OH$ or

30 $COO(CH_2)_q OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, ..

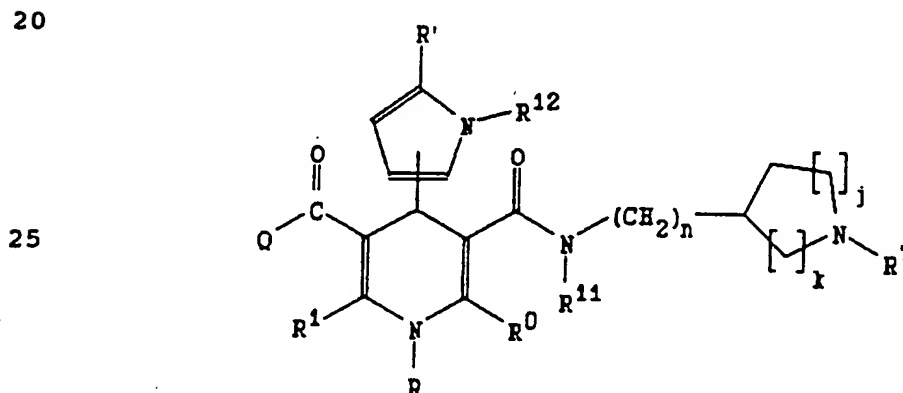
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quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
 OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where
 R' is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R¹¹ is H or a linear chain alkyl group;
 15 wherein R¹² is H or a linear chain alkyl or acyl group;
 and wherein n is 2, 3 or 4.

In addition, the invention provides a compound having the
 structure:



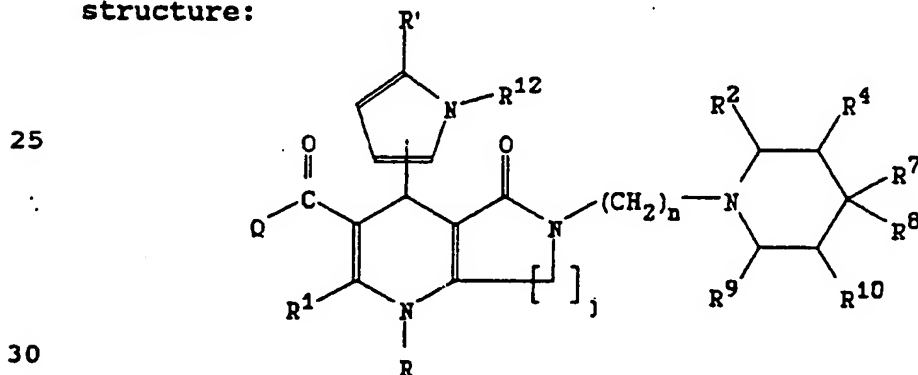
30 wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂''',
 NR''OH, NR''OR''', or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl
 group, or an aryl group, where R'' is H, a linear or
 branched chain alkyl group, trialkylsilylalkyl,
 35 cyanoalkyl, or an aryl group, and R''' is a linear or
 branched chain alkyl group, or an aryl group; wherein R⁰,
 R¹ and R' are independently the same or different and are

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H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 is an aryl or diarylalkyl group; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

20

The invention also provides a compound having the structure:



wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR'''OH$, $NR'''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^1

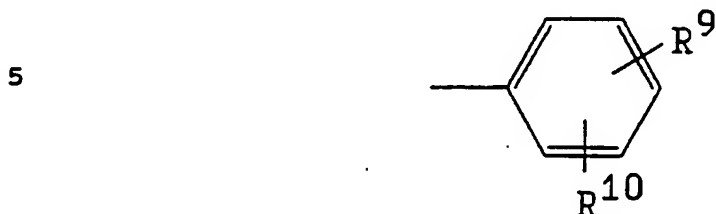
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and R' are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R¹ and R' are independently the same or different and are H, or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)₄OH or COO(CH₂)₄OR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl,

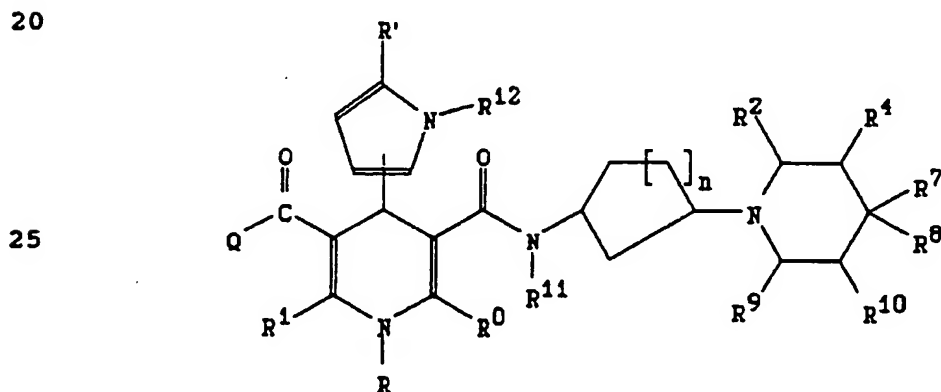
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indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR^v_2 , NHCOR^v , NHCOOR^v or NHCONHR^v , where R^v is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; wherein j is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

The invention further provides a compound having the structure:

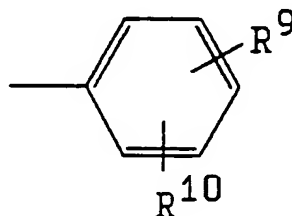


30 wherein Q is OH, $\text{OR}^{''}$, SH, $\text{SR}^{'''}$, NH_2 , $\text{NHR}^{'''}$, $\text{NR}_2^{'''}$, $\text{NR}^{''}\text{OH}$, $\text{NR}^{''}\text{OR}^{'''}$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where $R^{''}$ is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and $R^{'''}$ is a linear or branched chain alkyl group, or an aryl group; wherein R^0 , R^1 and R^v are independently the same or different and are

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H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2 W^0 (CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_q OH$ or $COO(CH_2)_q OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

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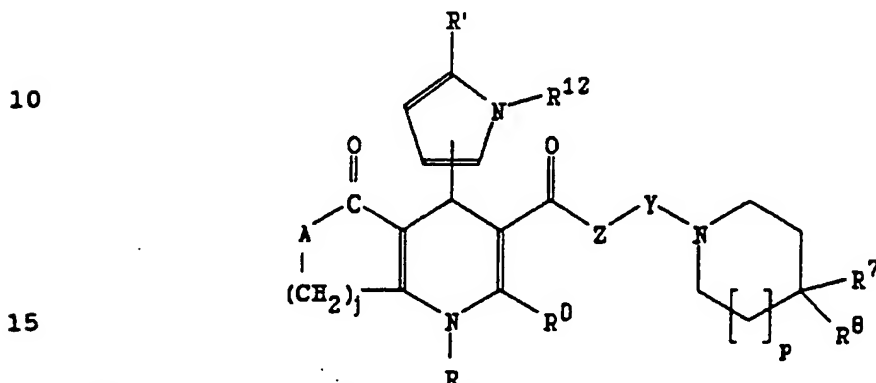
wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is

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a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; and wherein n is 0, 1, 2, 3 or 4.

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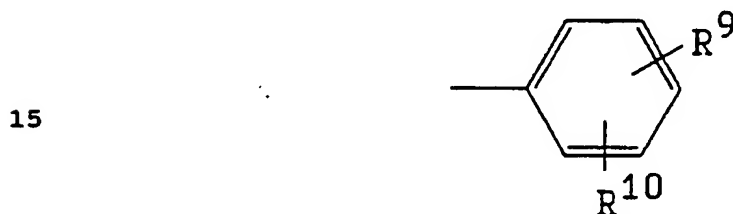
The invention further provides a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH_2 , CR^a_2 , NH , NR^a , $NCHO$, $NCOR^a$, NOH , O or S , where R^a is a methyl, ethyl or propyl group; wherein Z is O , NH , $NCHO$, $NCOR^b$, NR^b , NOR^b , or CH_2 , where R^b is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R' are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_w$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_w^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O , S or NH , where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched

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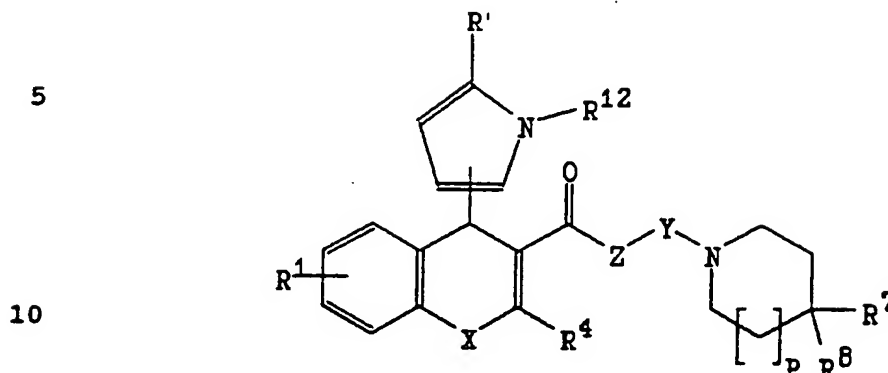
chain alkyl group, or an aryl group, where Z is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, ORⁿ, OCORⁿ, OCOORⁿ, OCONHRⁿ, NH₂, NHRⁿ, NRⁿ₂, NHCORⁿ, NHCOORⁿ or NHCONHRⁿ, where R' is a linear or branched chain alkyl group, and Rⁿ is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² is H or a linear chain alkyl or acyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

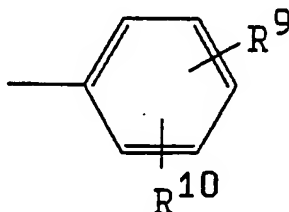
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The invention still further provides a compound having the structure:



wherein X is NH, NR^a, O, or S, where R^a is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -O-(CH₂)_h-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR', or CH₂, where R' is a methyl, ethyl or propyl group; wherein R^a is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)₄OH or COO(CH₂)₄OR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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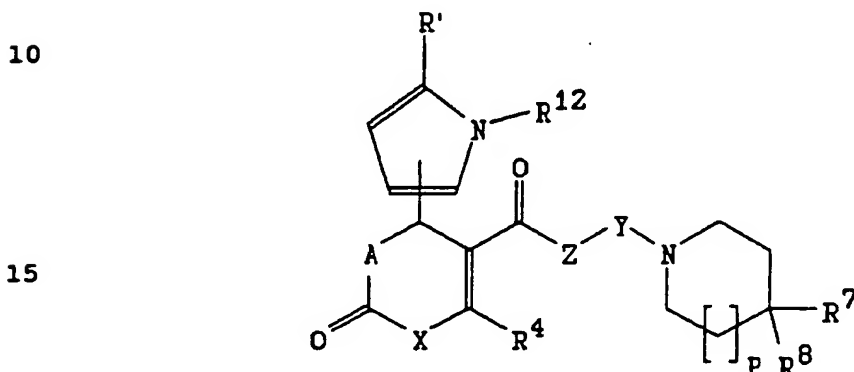
35

wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^w, OCOR^w, OCOOR^w,

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$\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and
 5 wherein p is 0, 1, 2 or 3.

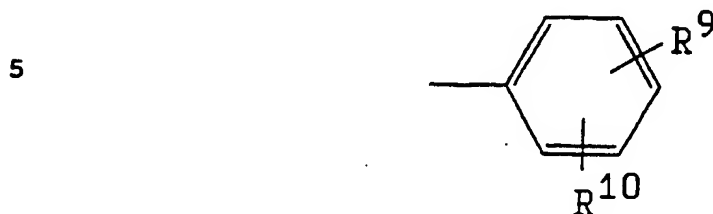
The invention also provides a compound having the structure:



wherein A is CH_2 , CR' , NH , NR' , NCHO , NCOR' , NOH , O or S , where R' is a methyl, ethyl or propyl group; wherein Y is
 20 $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR'' , NR'' ,
 25 NOR'' , or CH_2 , where R'' is a methyl, ethyl or propyl group; wherein X is NH , NR' , O , or S , where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^1 is H, or a methyl, ethyl or propyl group; wherein R^4 is H, or a linear or branched chain
 30 alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR' , NHCOR' , CONH_2 , CONHR' , CONR' , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched
 35 chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,

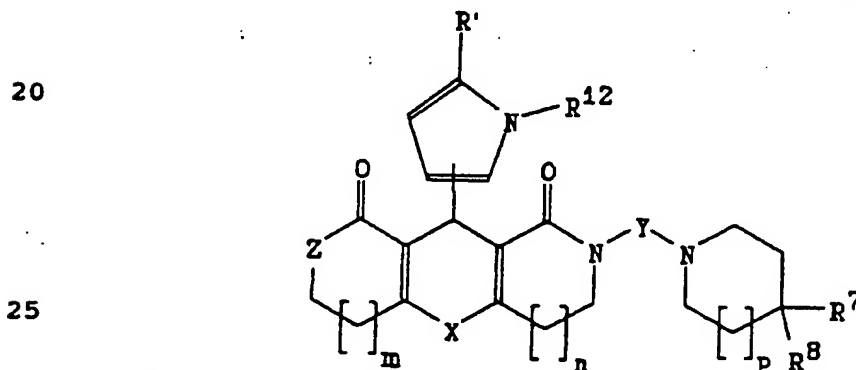
-113-

quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N, OR^v , OCOR^v , OCOOR^v ,
 OCONHR^v , NH_2 , NHR^v , NR^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where
 R^v is a linear or branched chain alkyl group, and R^w is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R^{12} is H or a linear chain alkyl or acyl
 15 group; and wherein p is 0, 1, 2 or 3.

The invention provides a compound having the structure:

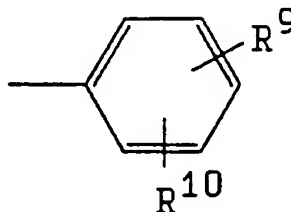


wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-$
 $\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or
 different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or
 30 $(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the
 same or different and are 1, 2, 3 or 4; wherein Z is O,
 NH, NCHO, NCOR^v , NR^v , NOR^v , or CH_2 , where R^v is a methyl,
 ethyl or propyl group; wherein X is NH, $\text{NR}^{v'}$, O, or S,
 where $R^{v'}$ is H or a linear or branched chain alkyl or
 35 acyl group, or an aryl group; wherein R^v is H, or a
 methyl, ethyl or propyl group; wherein R^7 and R^8 are
 independently the same or different and are H, CN, CF_3 ,

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OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR',
 CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or
 COO(CH₂)_qOR', or a benzyl group, a linear or branched
 chain alkyl or cycloalkyl group, or are a heteroaryl
 5 group comprising a pyridyl, indolyl, indolylalkyl,
 quinoliny, isoquinoliny, pyrrol, furyl or thiophene
 group, or an aryl group having the structure:

10

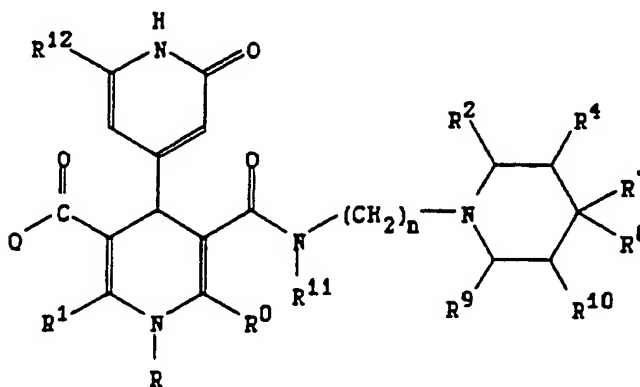


wherein R⁹ and R¹⁰ are independently the same or different
 15 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
 OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where
 R' is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R¹² is H or a linear chain alkyl or acyl
 20 group; wherein m and n are independently the same or
 different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

The invention also provides a compound having the
 structure:

25

30



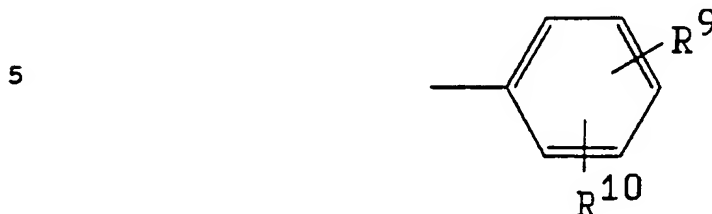
35 wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR''₂,
 NR''OH, NR''OR'', or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl

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group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 ,
 5 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$,
 10 $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$,
 15 $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl
 20 group; wherein R^0 and R^1 are independently the same or different and are H, or a linear or branched chain alkyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear
 25 or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$,
 30 $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl,

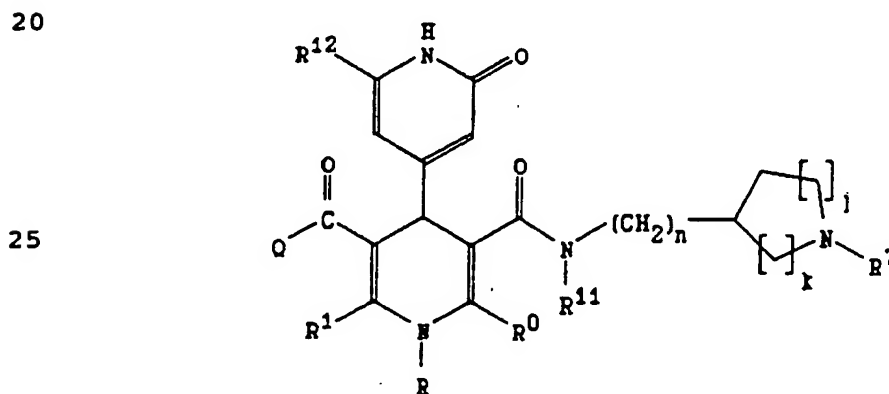
-116-

indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where R^v is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group;
 15 wherein R^{12} is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

The invention further provides a compound having the structure:



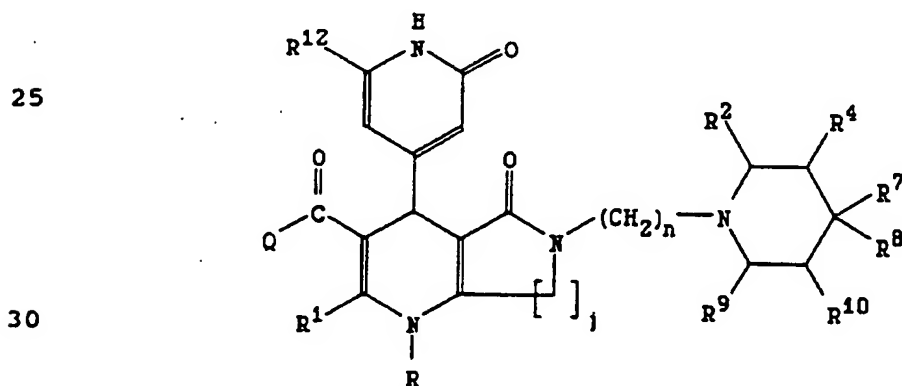
30 wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl,
 35 cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H or a linear or branched chain alkyl or acyl group,

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or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2 W^0 (CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 is an aryl or diarylalkyl group; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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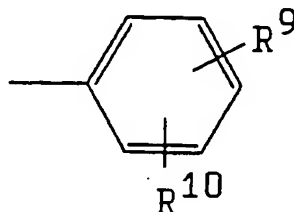
The invention still further provides a compound having the structure:



wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl,

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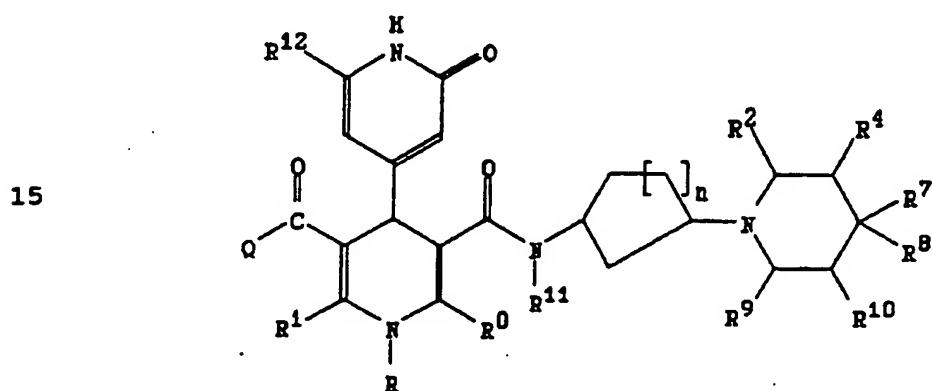
cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_q OH$ or $COO(CH_2)_q OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR_2^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

The invention also provides a compound having the structure:

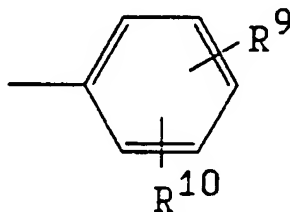


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_j\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_j\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$,

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NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

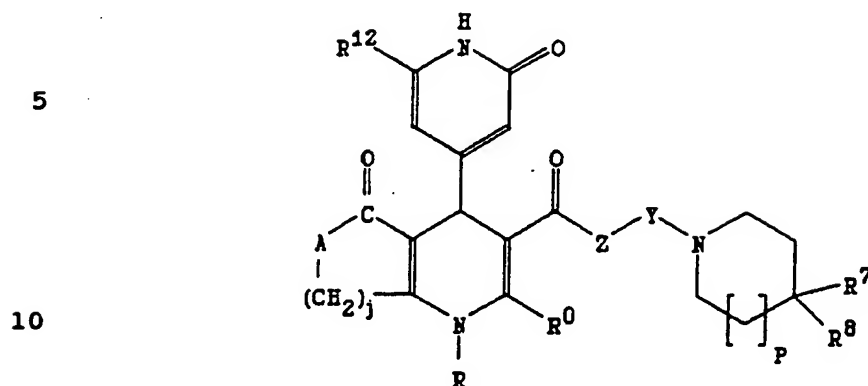
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wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR'', OCOR'', OCOOR'', OCONHR'', NH₂, NHR'', NR'', NHCOR'', NHCOOR'' or NHCONHR'', where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl or acyl group; and wherein n is 0, 1, 2, 3 or 4.

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The invention further provides a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-$, $O-(CH_2)_k-$, where h and k are independently the same or
 15 different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH_2 , CR'_2 , NH , NR' , $NCHO$, $NCOR'$, NOH , O or S , where R' is a methyl, ethyl or propyl group; wherein Z is O , NH , $NCHO$,
 20 $NCOR''$, NR'' , NOR'' , or CH_2 , where R'' is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl,
 25 trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear
 30 or branched chain alkyl group, or an aryl group, where W^0 is O , S or NH , where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3,
 35 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$,

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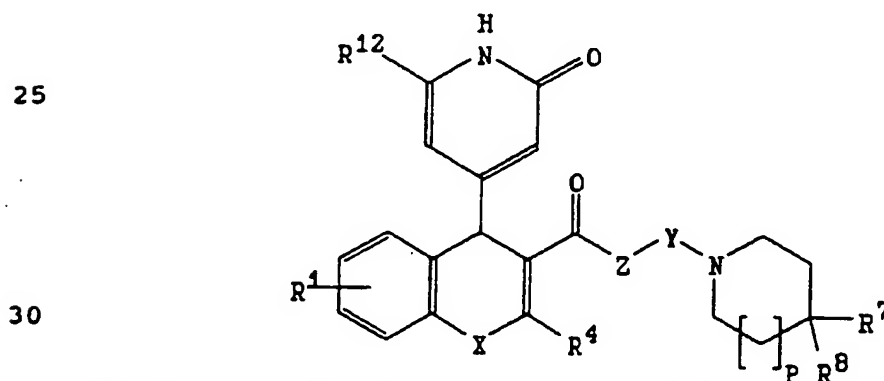
CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or
 COO(CH₂)_qOR', or a benzyl group, a linear or branched
 chain alkyl or cycloalkyl group, or are a heteroaryl
 group comprising a pyridyl, indolyl, indolylalkyl,
 5 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
 15 OCONHR^v, NH₂, NHR^v, NR^v, NHCOR^v, NHCOOR^v or NHCONHR^v, where
 R' is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R¹² is H or a linear chain alkyl group;
 wherein j is 1, 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

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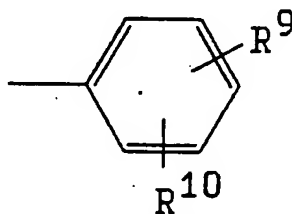
The invention also provides a compound having the
 structure:



wherein X is NH, NR'', O or S, where R'' is H or a linear
 or branched chain alkyl or acyl group, or an aryl group;
 wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-
 35 O-(CH₂)_k-, where h and k are independently the same or
 different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -
 (CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the

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same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein R¹ is H, Cl, Br, I, F, NO₂, CN, OH, OR², OCOR², NH₂, NR², NHCOR₂, or CF₃, where R² is a
 5 linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂,
 10 COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 15 group, or an aryl group having the structure:

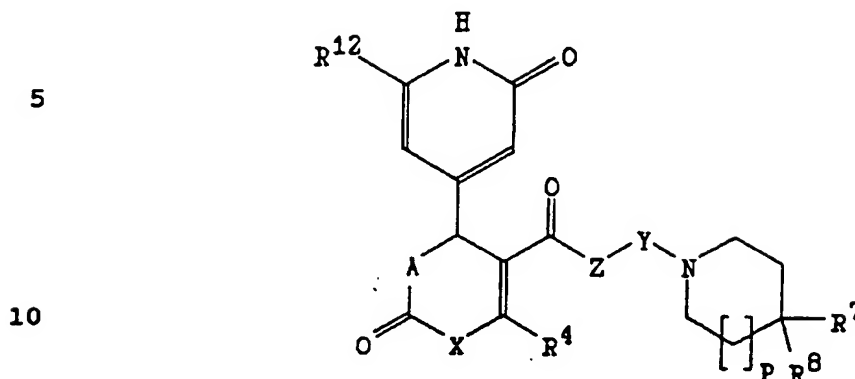


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wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^w, OCOR^w, OCOOR^w, OCONHR^w, NH₂, NHR^w, NR^w₂, NHCOR^w, NHCOOR^w or NHCONHR^w, where
 25 R' is a linear or branched chain alkyl group, and R^w is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

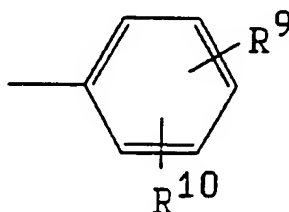
-124-

The invention further provides a compound having the structure:



wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein X is NH , NR'' , O or S , where R'' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

35



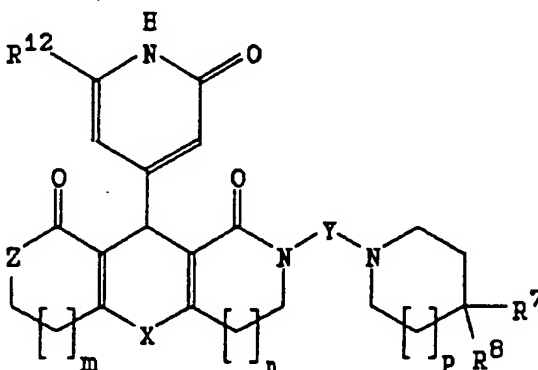
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

The invention provides a compound having the structure:

10

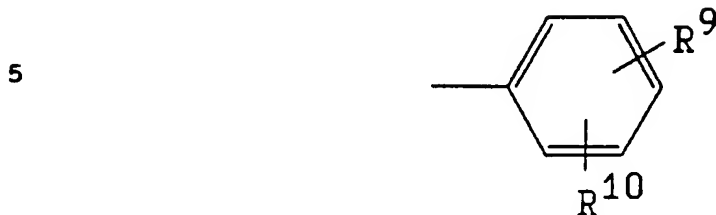
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wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-$ $\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}=\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein X is NH, NR' , O, or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR_2' , NHCOR' , CONH_2 , CONHR' , CONR_2' , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquin-

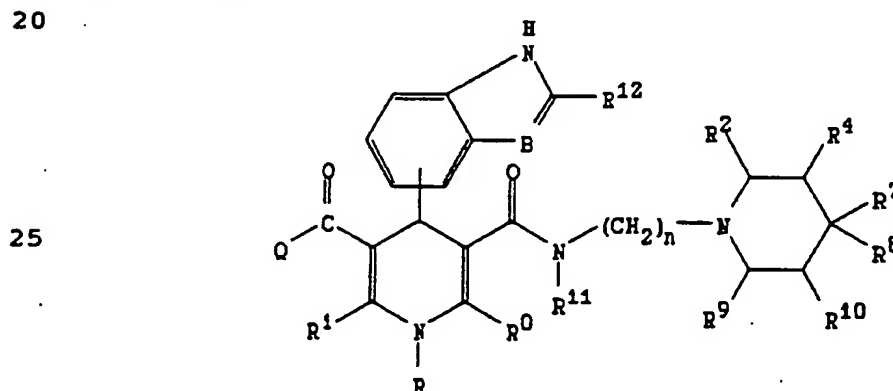
-126-

oliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR_2^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where R^v is a linear or branched chain alkyl group, and R^w is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

The invention also provides a compound having the structure:

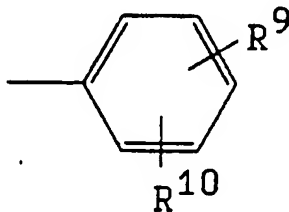


30 wherein B is CH or N; wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and
35 R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same

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or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2 W^0 (CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_4 OH$ or $COO(CH_2)_4 OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

30

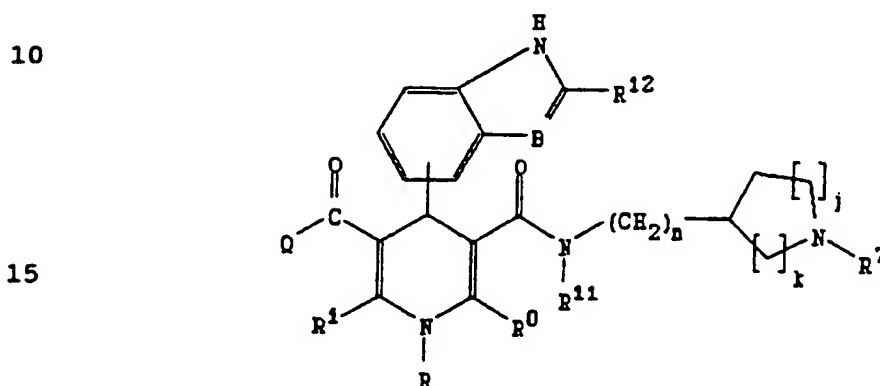


35 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $CONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where

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R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; and
 5 wherein n is 2, 3 or 4.

The invention further provides a compound having the structure:

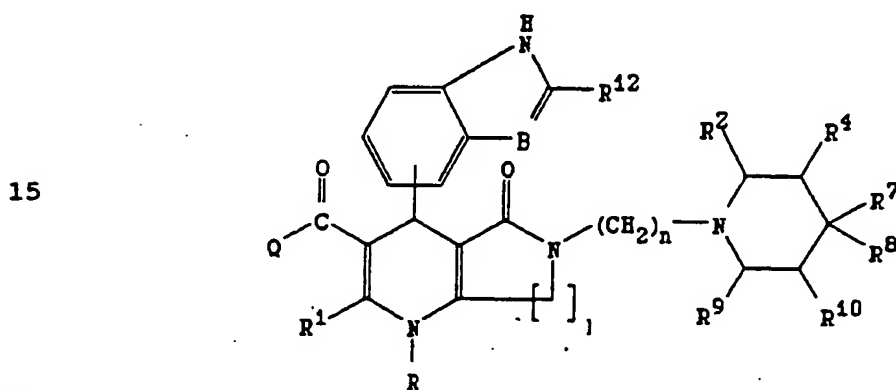


wherein B is CH or N; wherein Q is OH, OR'', SH, SR'',
 20 NH₂, NHR'', NR₂'', NR''OH, NR''OR'', or a linear or
 branched chain alkyl group, or an arylalkyl group, or an
 alkenyl or alkynyl group, or an aryl group, where R'' is
 H, a linear or branched chain alkyl group,
 trialkylsilylalkyl, cyanoalkyl, or an aryl group, and
 25 R''' is a linear or branched chain alkyl group, or an
 aryl group; wherein R⁰ and R¹ are independently the same
 or different and are H, a linear or branched chain alkyl,
 an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-
 alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxy-
 30 alkyl, or an aryl group, or (CH₂)_iW, where W is NH₂, NHR',
 NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_kW¹, or a
 linear or branched chain alkyl group, or an arylalkyl
 group, or an alkenyl or alkynyl group, or an aryl group,
 where R' is a linear or branched chain alkyl group, or an
 35 aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR',
 NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a
 linear or branched chain alkyl group, or an aryl group,

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where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 is an aryl or diarylalkyl group; wherein R^{11} is a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

The invention still further provides a compound having the structure:

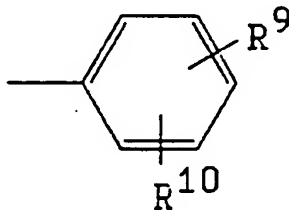


wherein B is CH or N; wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR₂'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R'' is a

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linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

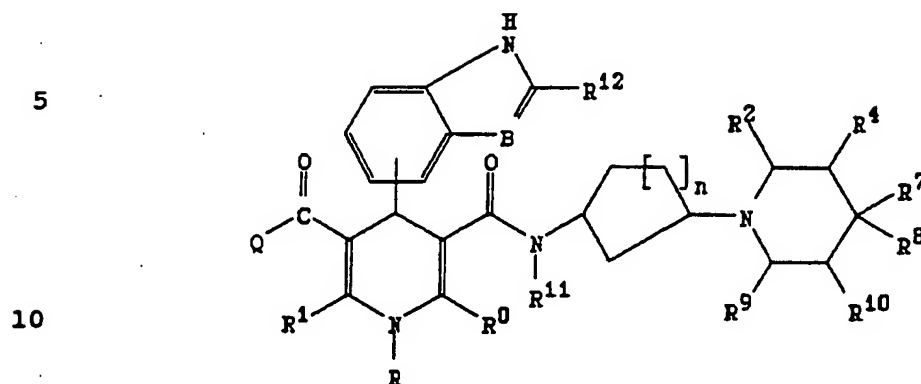
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25 wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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The invention also provides a compound having the structure:



wherein B is CH or N; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group;

15 wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR',

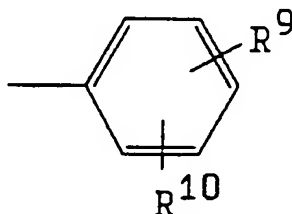
25 NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group,

30 or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched

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chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 ,
 5 OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,
 10 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

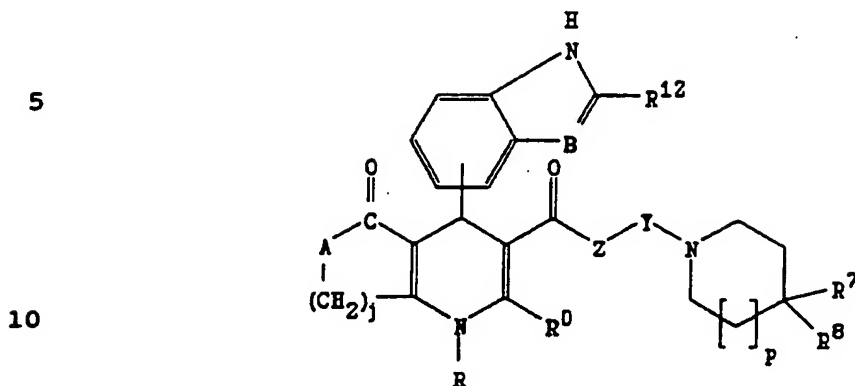
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$,
 20 $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group;
 25 and n is 2, 3 or 4.

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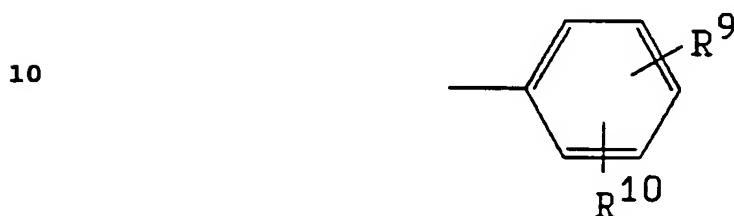
The invention further provides a compound having the structure:



wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein B is
 15 CH or N ; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O ,
 20 NH , NCHO , NCOR , NR , NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^0 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_t\text{W}$,
 25 where W is NH_2 , NHR' , NR'_2 , NHOH , $\text{N}^+\text{R}'_3\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O , S or NH ,
 30 where W^1 is NH_2 , NHR' , NR'_2 , NHOH , $\text{N}^+\text{R}'_3\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group;
 35 wherein R^7 and R^8 are independently the same or different and are H, CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR'_2 ,

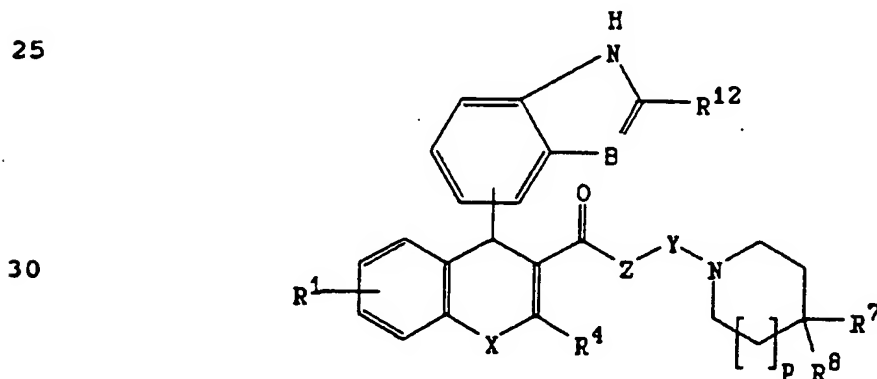
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NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

The invention still further provides a compound having the structure:

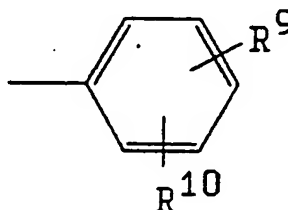


wherein B is CH or N; wherein X is NH, NR', O, or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4;

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$-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH₂, where R is a methyl, ethyl or propyl group; wherein R¹ is
 5 H, Cl, Br, I, F, NO₂, CN, OH, OR², OCOR², NH₂, NR², NHCOR₂ or CF₃, where R² is a linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H,
 10 CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl,
 15 indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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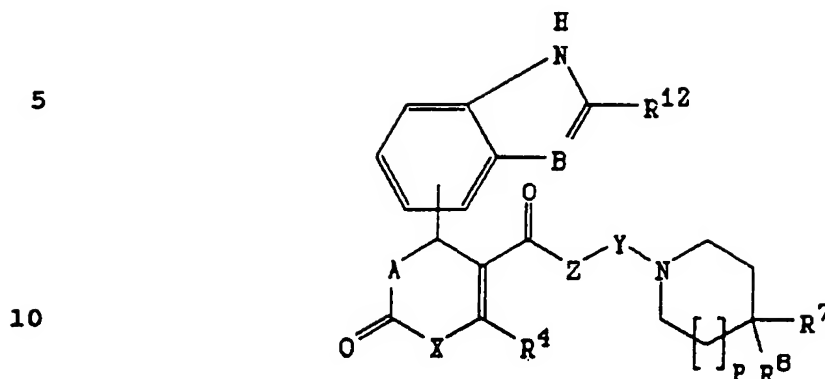


wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
 25 OCONHR^v, NH₂, NHR^v, NR₂^v, NHCOR^v, NHCOOR^v or NHCONHR^v, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

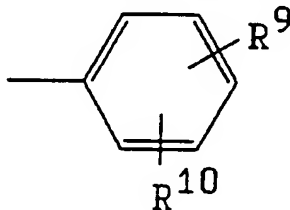
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The invention also provides a compound having the structure:

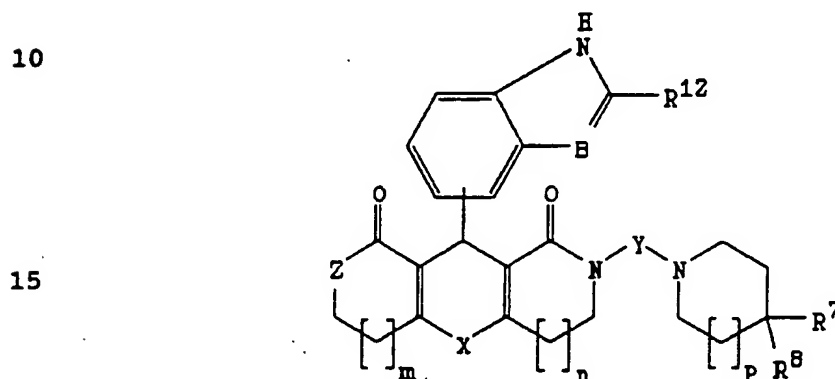


wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; B is CH or N ; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR , NR , NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein X is NH , NR' , O or S , where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



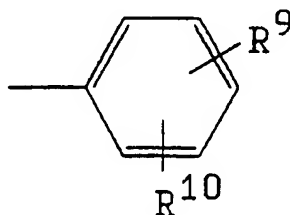
-137-

wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and
 5 R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3. The invention further provides a compound having the structure:



wherein B is CH or N; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are
 20 independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein X is
 25 NH, NR' , O or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH, COOR' , CHO, COR' , COSH, COSR' ,
 30 $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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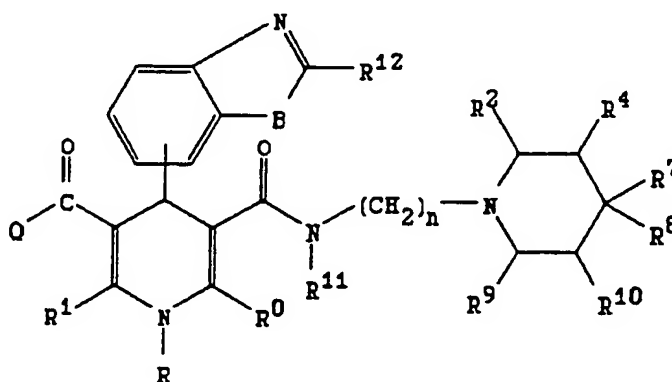
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5 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4
 10 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

The invention provides a compound having the structure:

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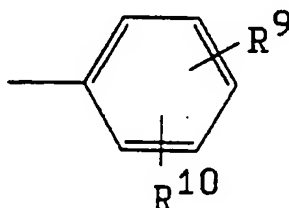


25 wherein B is O or S; wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkyl-
 30 silylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-
 35 alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_p\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_p\text{W}^1$, or a

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linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' ,
 5 NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group,
 10 or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or
 15 branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched
 20 chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

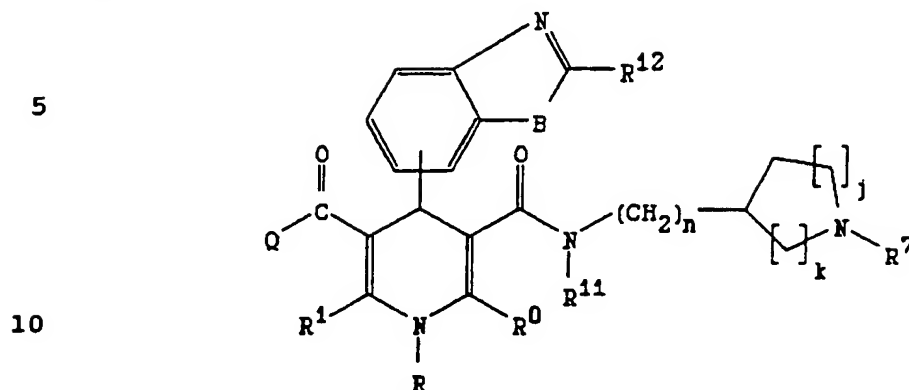
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30 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $CONHR^v$, NH_2 , NHR^v , NR_2^v , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4
 35 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; and n is 2, 3 or 4.

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The invention also provides a compound having the structure:

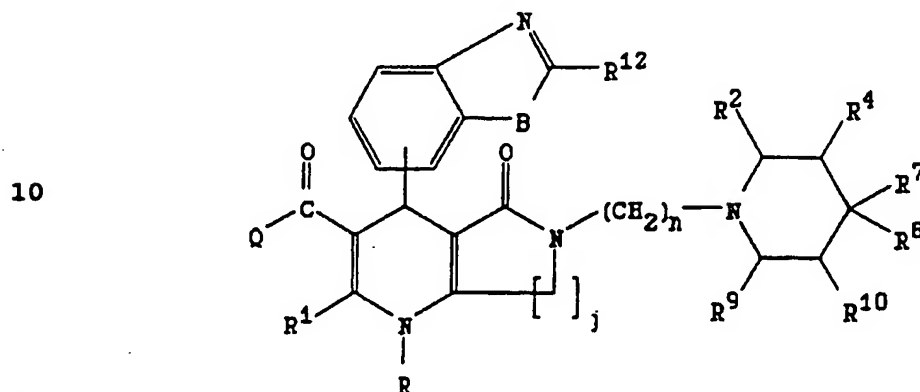


wherein B is O or S; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or
 15 branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group;
 20 wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a
 25 linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a
 30 linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁷ is an aryl or diarylalkyl group; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; wherein j

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and k are independently the same or different and are 0, 1, 2, 3 or 4; and n is 2, 3 or 4.

The invention further provides a compound having the structure:

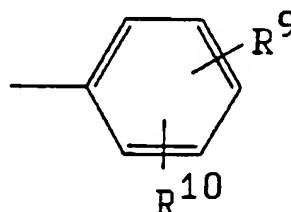


wherein B is O or S; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z', NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z', NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently

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the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

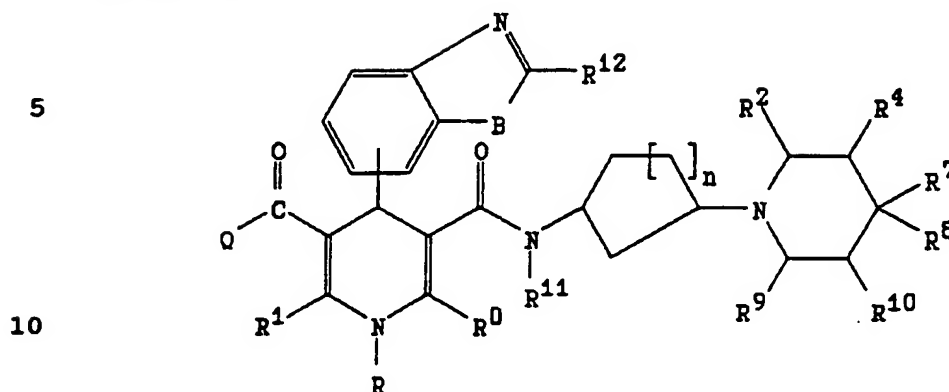
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20 wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, ORⁿ, OCORⁿ, OCOORⁿ, OCONHRⁿ, NH₂, NHRⁿ, NRⁿ₂, NHCORⁿ, NHCOORⁿ or NHCONHRⁿ, where R' is a linear or branched chain alkyl group, and Rⁿ is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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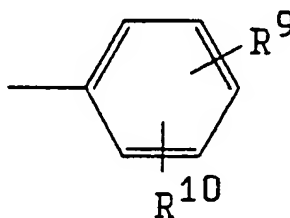
The invention still further provides a compound having the structure:



wherein B is O or S; wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR₂'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl or alkoxyethyl group, or a

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hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$,
 5 $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 10 group, or an aryl group having the structure:



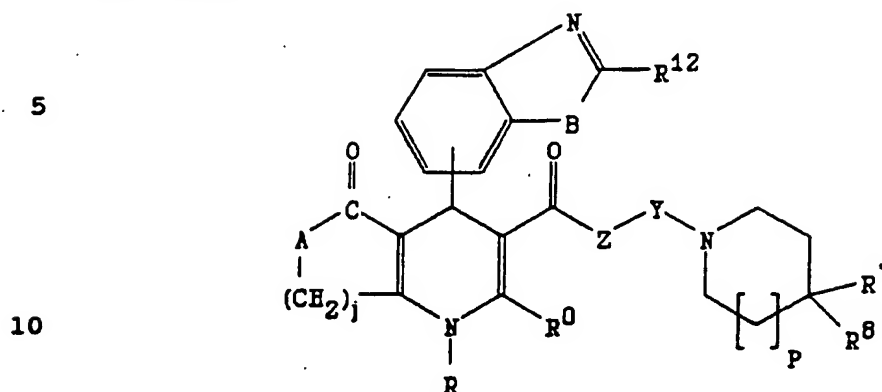
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where
 20 R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; and wherein n is 0, 1, 2, 3 or 4.

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In addition, the invention provides a compound having the structure:

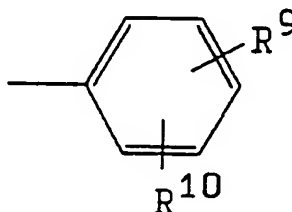


wherein B is O or S; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH₂, CR', NH, NR', NCHO, NCOR', NOH, O or S, where R' is a methyl, ethyl or propyl

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group; wherein Z is O, NH, NCHO, NCOR', NR', NOR', or CH₂, where R' is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

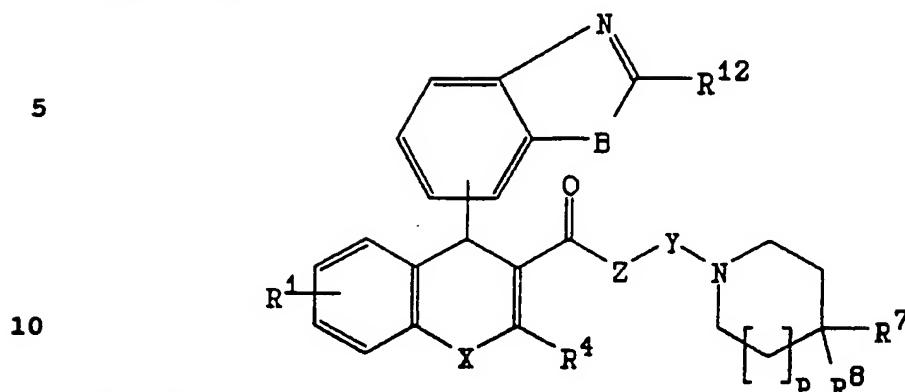
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wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, ORⁿ, OCORⁿ, OCOORⁿ, OCONHRⁿ, NH₂, NHRⁿ, NRⁿ₂, NHCORⁿ, NHCOORⁿ or NHCONHRⁿ, where R' is a linear or branched chain alkyl group, and Rⁿ is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

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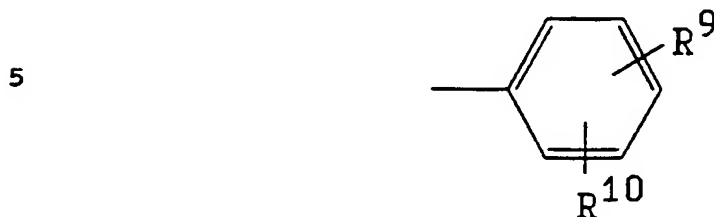
The invention also provides a compound having the structure:



wherein B is O or S; wherein X is NH, NR', O, or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH₂, where R is a methyl, ethyl or propyl group; wherein R¹ is H, Cl, Br, I, F, NO₂, CN, OH, OR², OCOR², NH₂, NR², NHCOR₂, or CF₃, where R² is a linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR', NHCOR', CONH₂, CONHR', CONR', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl,

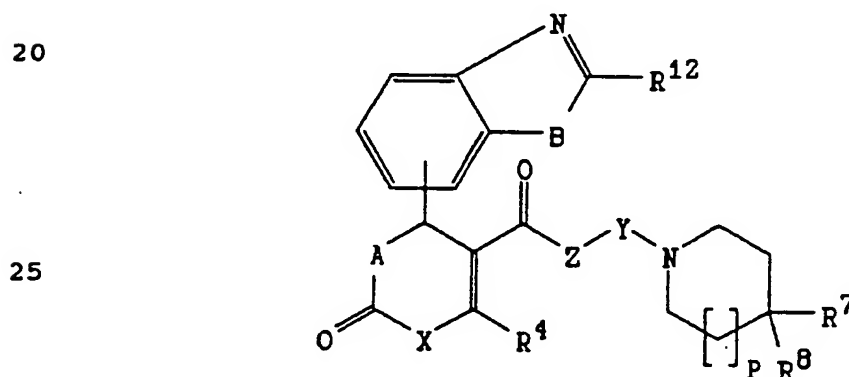
-148-

indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^n , OCOR^n , OCOOR^n ,
 OCONHR^n , NH_2 , NHR^n , NR^n_2 , NHCOR^n , NHCOOR^n or NHCONHR^n , where
 R' is a linear or branched chain alkyl group, and R^n is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R^{12} is H or a linear chain alkyl group; and
 15 wherein p is 0, 1, 2 or 3.

The invention further provides a compound having the structure:

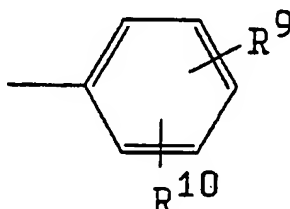


wherein A is CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S,
 30 where R is a methyl, ethyl or propyl group; wherein B is
 O or S; wherein X is NH, NR' , O, or S, where R' is H or
 a linear or branched chain alkyl or acyl group, or an
 aryl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4
 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently
 35 the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-$
 $(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are
 independently the same or different and are 1, 2, 3 or 4;

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wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH₂, where R is a methyl, ethyl or propyl group; wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different
 5 and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl,
 10 indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

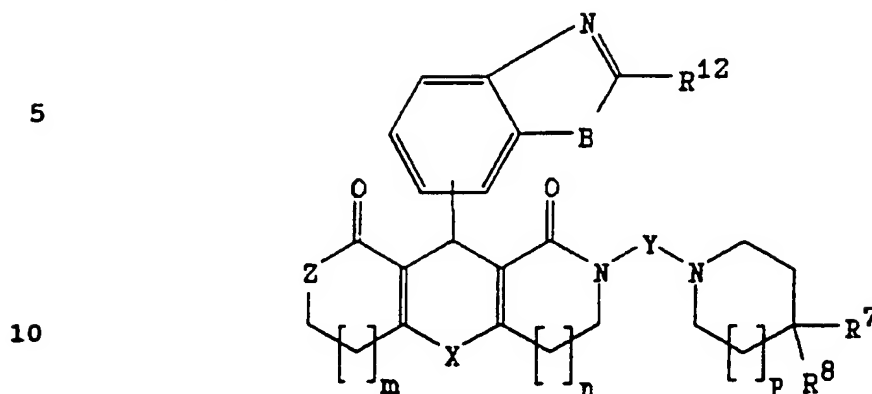
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wherein R⁹ and R¹⁰ are independently the same or different
 20 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² is H or a linear chain alkyl group; and
 25 wherein p is 0, 1, 2 or 3.

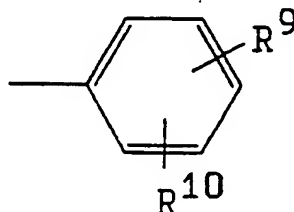
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The invention still further provides a compound having the structure:



wherein B is O or S; wherein X is NH, NR', O or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH₂, where R is a methyl, ethyl or propyl group; wherein R' and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)₄OH or COO(CH₂)₄OR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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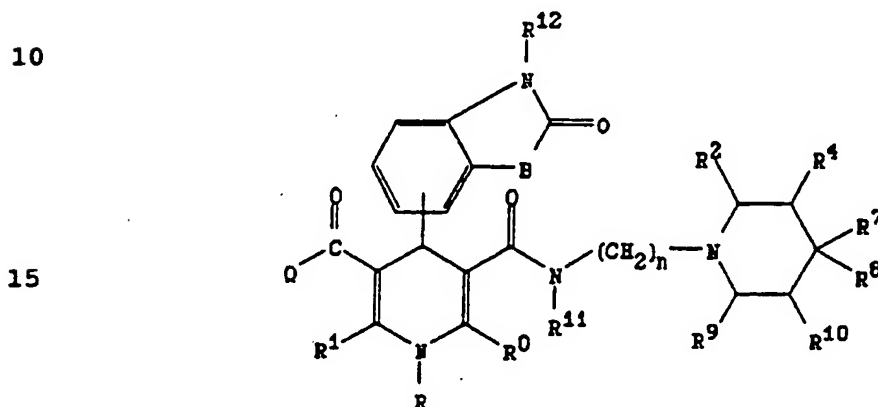
wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^w, OCOR^w, OCOOR^w,

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OCONHR^{v} , NH_2 , NHR^{v} , NR^{v} , NHCOR^{v} , NHCOOR^{v} or $\text{NHCONHR}^{\text{v}}$, where R' is a linear or branched chain alkyl group, and R^{v} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group;

5 wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

The invention provides a compound having the structure:



wherein B is O, S or NR^{12} ; wherein Q is OH, OR'' , SH,

20 SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a

25 linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_p\text{W}$, where W is NH_2 , NHR' ,

30 NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_p\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an

35 aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group,

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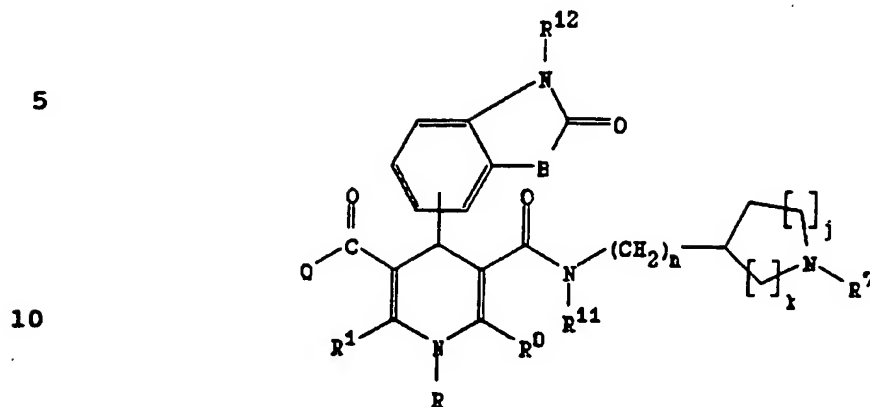
where Z is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, ORⁿ, OCORⁿ, OCOORⁿ, OCONHRⁿ, NH₂, NHRⁿ, NRⁿ₂, NHCORⁿ, NHCOORⁿ or NHCONHRⁿ, where R' is a linear or branched chain alkyl group, and Rⁿ is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; and n is 2, 3 or 4.

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The invention also provides a compound having the structure:

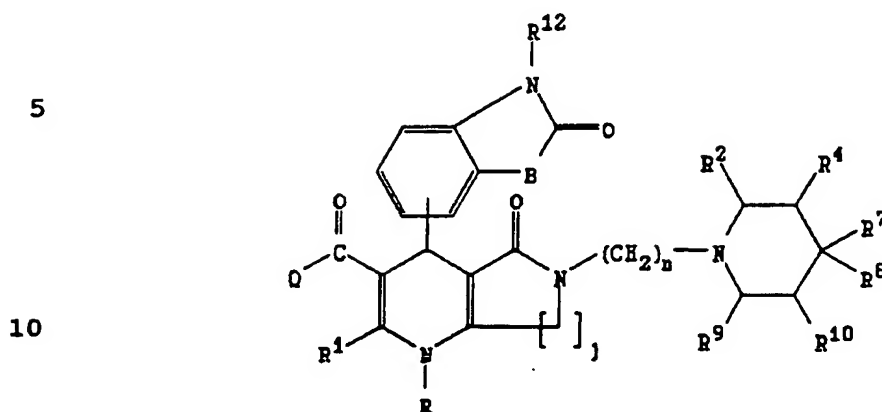


wherein B is O, S or N¹²; wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR₂'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group;

wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_nW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ is an aryl or diarylalkyl group; wherein R¹¹ is a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and n is 2, 3 or 4.

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The invention further provides a compound having the structure:

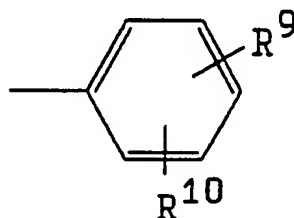


wherein B is O, S or N¹²; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a

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hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$,
 5 $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 10 group, or an aryl group having the structure:

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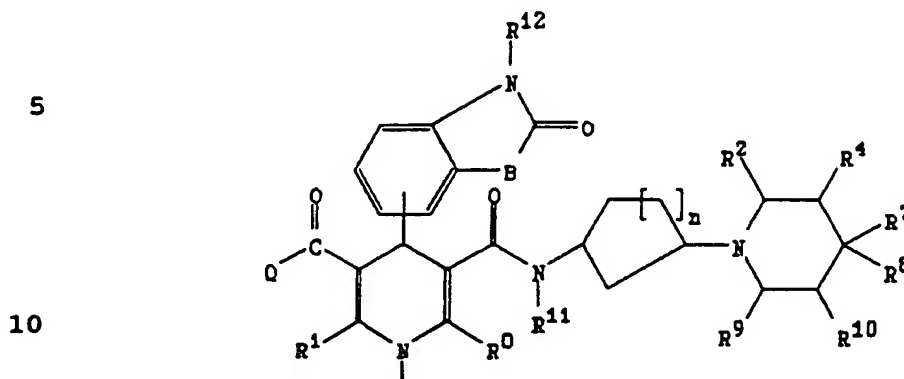


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where
 20 R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; and n is 2, 3 or 4.

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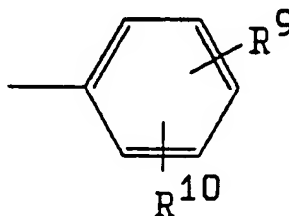
The invention still further provides a compound having the structure:



wherein B is CH or R^N ; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a

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hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$,
 5 $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 10 group, or an aryl group having the structure:



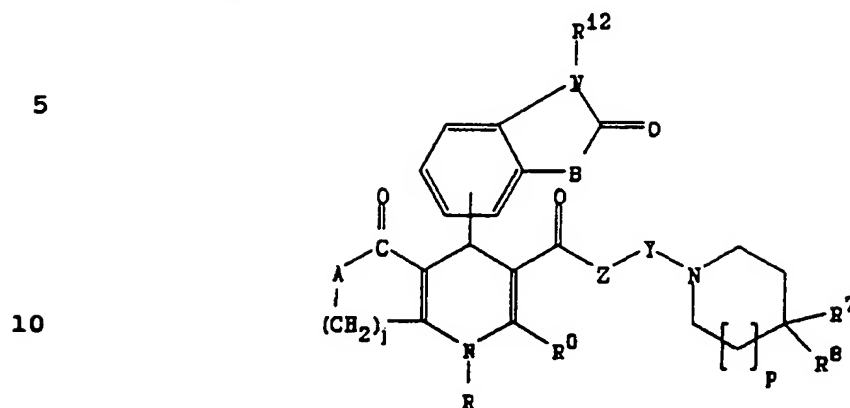
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where
 20 R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; wherein j is 1, 2, 3 or 4; and n is 0, 1, 2, 3 or 4.

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The invention also provides a compound having the structure:

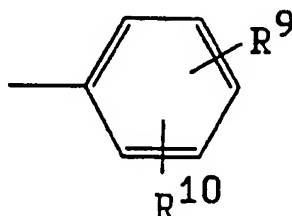


wherein B is O, S, or NR', where R' is H or a linear chain alkyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH_2 , CR^1 , NH, NR^1 , $NCHO$, $NCOR^1$, NOH , O or S, where R^1 is a methyl, ethyl or propyl group; wherein Z is O, NH, $NCHO$, $NCOR^2$, NR^2 , NOR^2 , or CH_2 , where R^2 is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 is independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR^3 , NR_2^3 , $NHOH$, $N^+R_3^3Z^-$, $NHCOR^3$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R^3 is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR^3 , NR_2^3 , $NHOH$, $N^+R_3^3Z^-$, $NHCOR^3$, N_3 or NO_2 , and where R^3 is a linear or branched chain alkyl group, or an aryl group, where Z is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein

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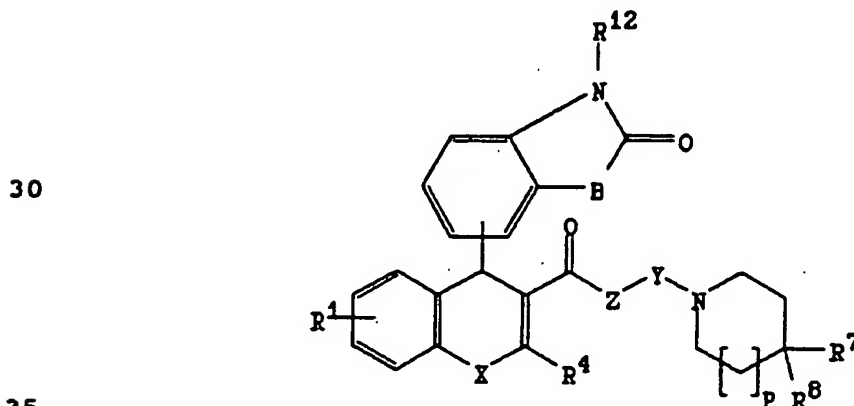
R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or
 5 branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

10



15 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N, OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4
 20 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

The invention further provides a compound having the
 25 structure:



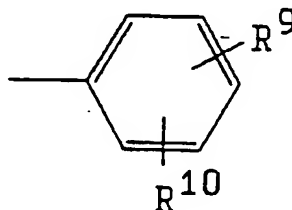
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wherein B is O, S or NR' , where R' is H or a linear chain alkyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4

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- or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4;
- 5 wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^1 is H, Cl, Br, I, F, NO_2 , CN, OH, OR^2 , $OCOR^2$, NH_2 , NR^2 , $NHCOR^2$ or CF_3 , where R^2 is a linear or branched chain alkyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain
- 10 alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched
- 15 chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

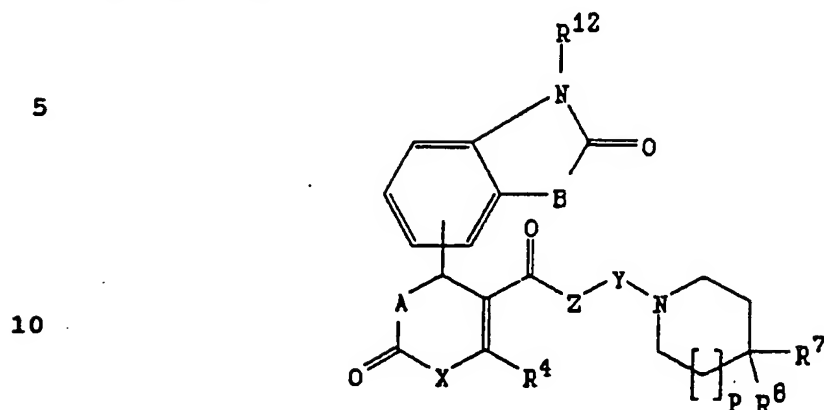
20



- 25 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N, OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R^v is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4
- 30 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

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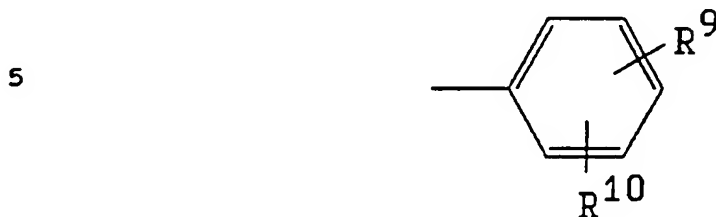
The invention still further provides a compound having the structure:



wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; B is O , S or NR' , where R' is H or a linear chain alkyl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR'' , NR'' , NOR'' or CH_2 , where R'' is a methyl, ethyl or propyl group; wherein X is NH , NR' , O or S , where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^4 is H , or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H , CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,

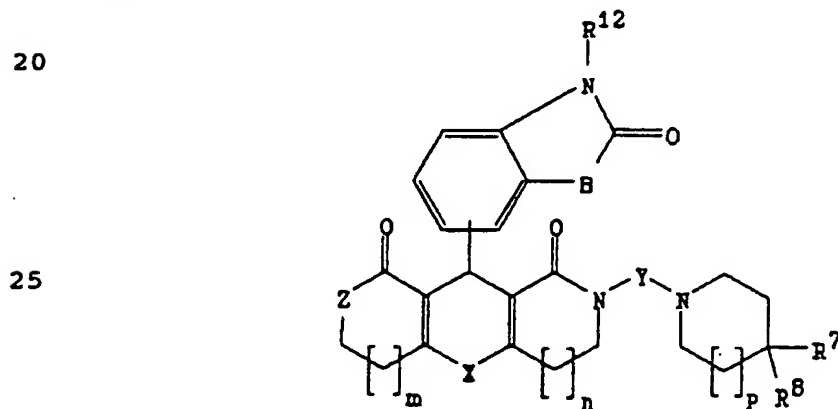
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quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v ,
 OCONHR^v , NH_2 , NHR^v , NR^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where
 R^v is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R^{12} is H or a linear chain alkyl group; and
 15 wherein p is 0, 1, 2 or 3.

The invention also provides a compound having the structure:

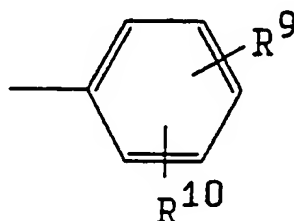


wherein B is O, S or NR' , where R' is H or a linear chain
 30 alkyl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4
 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently
 the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-$
 $(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are
 independently the same or different and are 1, 2, 3 or 4;
 35 wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is
 a methyl, ethyl or propyl group; wherein X is NH, NR' , O
 or S, where R' is H or a linear or branched chain alkyl

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or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or
 5 $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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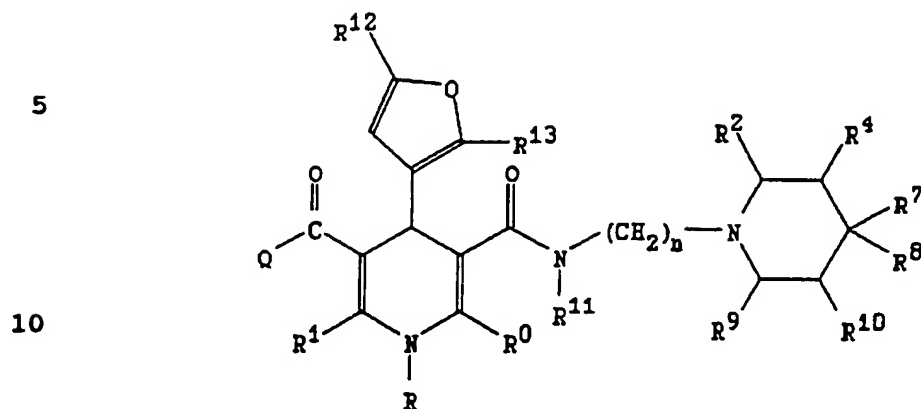


15

wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $CONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where
 20 R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

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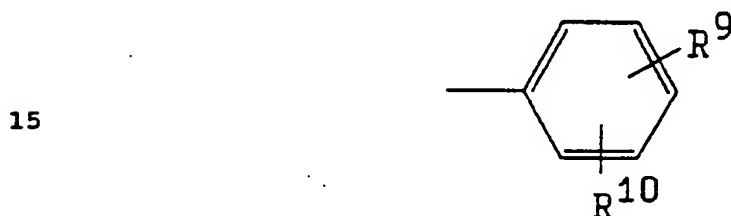
The invention further provides a compound having the structure:



wherein Q is OH , OR'' , SH , SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H , a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H , a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O , S or NH , where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain

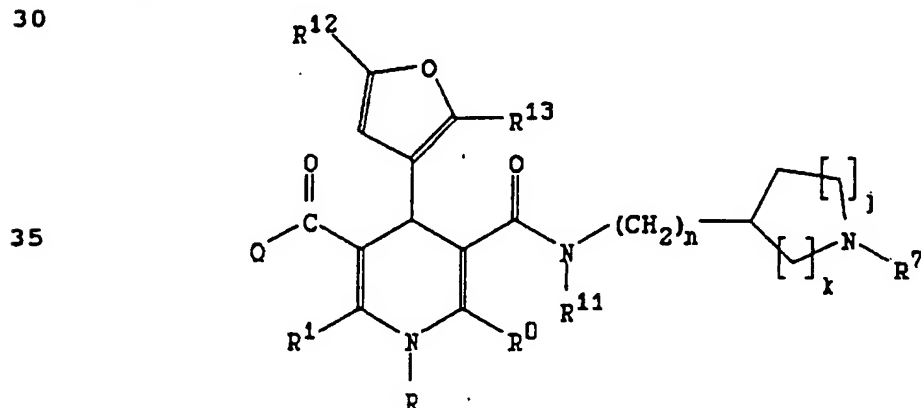
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alkyl, alkyloxymethyl or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' ,
 5 $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$,
 $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or
 $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,
 10 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N $_3$, OR'' , $OCOR''$, $OCOOR''$,
 20 $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where
 R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different
 25 and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

The invention still further provides a compound having the structure:



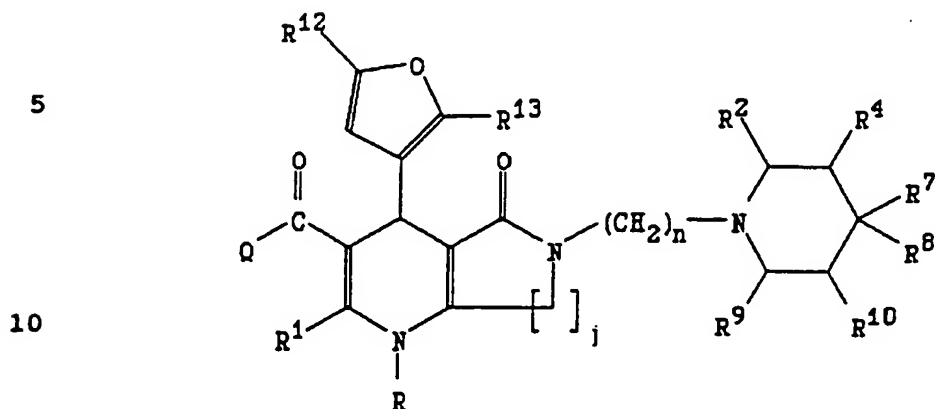
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wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁷ is an aryl or diarylalkyl group; wherein R¹¹ is a linear chain alkyl group; wherein R¹² and R¹³ are independently the same or different and are H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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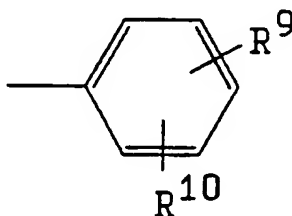
In addition, the invention provides a compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein Rⁱ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a

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hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$,
 5 $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene
 10 group, or an aryl group having the structure:

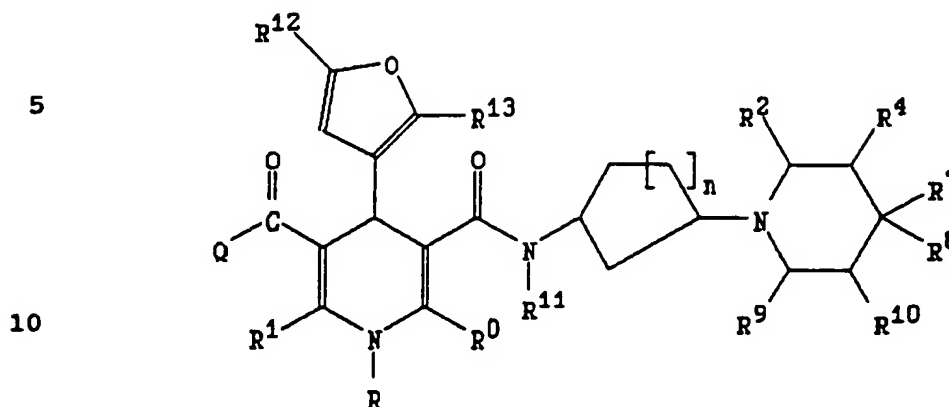


15

wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where
 20 R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is
 25 2, 3 or 4.

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The invention also provides a compound having the structure:

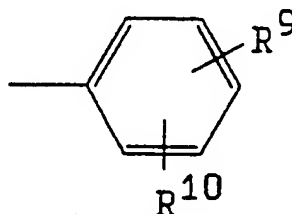


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are a linear or branched chain alkyl group; wherein R⁴ is a linear or branched chain alkyl, alkylox-

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ymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 ,
 5 NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$,
 CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquin-
 10 olinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

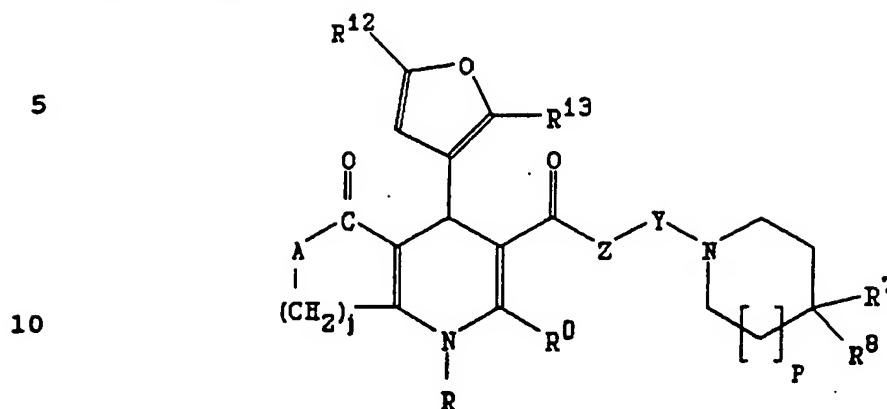
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$,
 20 $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where
 R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different
 25 and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 0, 1, 2, 3 or 4.

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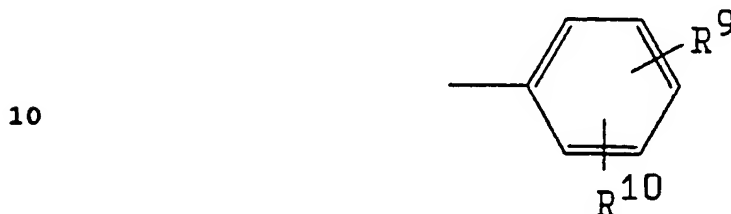
The invention further provides a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or
 15 different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH₂, CR'₂, NH, NR', NCHO, NCOR', NOH, O or S, where R' is a methyl, ethyl or propyl group; wherein Z is O, NH, NCHO,
 20 NCOR'', NR'', NOR'' or CH₂, where R'' is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl,
 25 trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR'₂', NHOH, N⁺R'₃'Z', NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear
 30 or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR'₂', NHOH, N⁺R'₃'Z', NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1, 2, 3,
 35 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂', NHCOR', CONH₂, CONHR',

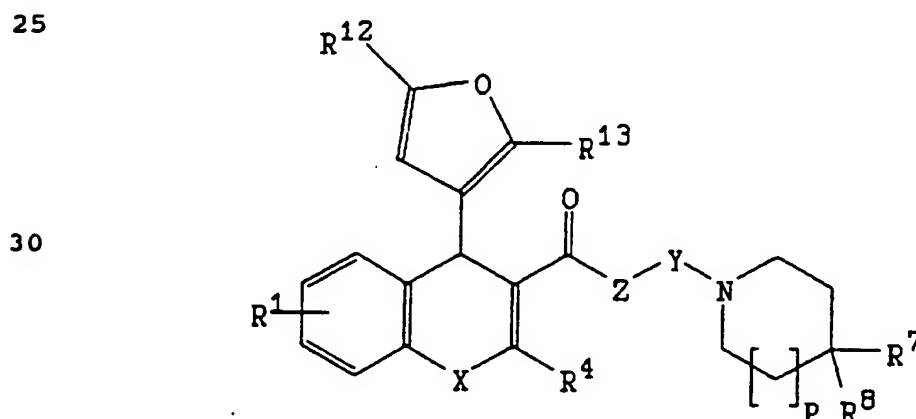
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CONR₂' , COOH, COOR' , CHO, COR' , COSH, COSR' , COO(CH₂)_qOH or
 COO(CH₂)_qOR' , or a benzyl group, a linear or branched
 chain alkyl or cycloalkyl group, or are a heteroaryl
 group comprising a pyridyl, indolyl, indolylalkyl,
 5 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
 15 OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where
 R' is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R¹² and R¹³ are independently the same or
 different and are H or a linear chain alkyl group;
 20 wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and
 wherein p is 0, 1, 2 or 3.

The invention still further provides a compound having
 the structure:

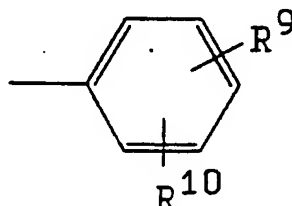


35 wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-
 O-(CH₂)_k-, where h and k are independently the same or
 different and are 2, 3 or 4; -(CH₂)_b-CH=CH-(CH₂)_k-; or -

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$(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^1 is H, Cl, Br, I, F, NO_2 , CN, OH, OR^2 , OCOR^2 , NH_2 , NR^2 , NHCOR^2 , or CF_3 , where R^2 is a linear or branched chain alkyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

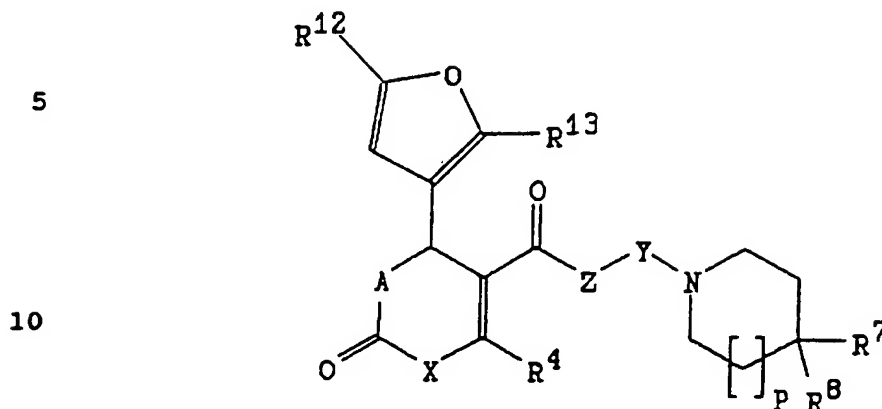
20



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^w , OCOR^w , OCOOR^w , OCONHR^w , NH_2 , NHR^w , NR^w_2 , NHCOR^w , NHCOOR^w or NHCONHR^w , where R' is a linear or branched chain alkyl group, and R^w is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

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The invention also provides a compound having the structure:



wherein A is CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein Y is

15 -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR',

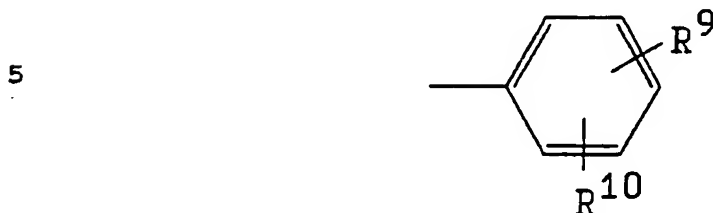
20 NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein X is NH, NR'', O or S, where R'' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independ-

25 ently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)₄OH or COO(CH₂)₄OR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl

30 group comprising a pyridyl, indolyl, indolylalkyl,

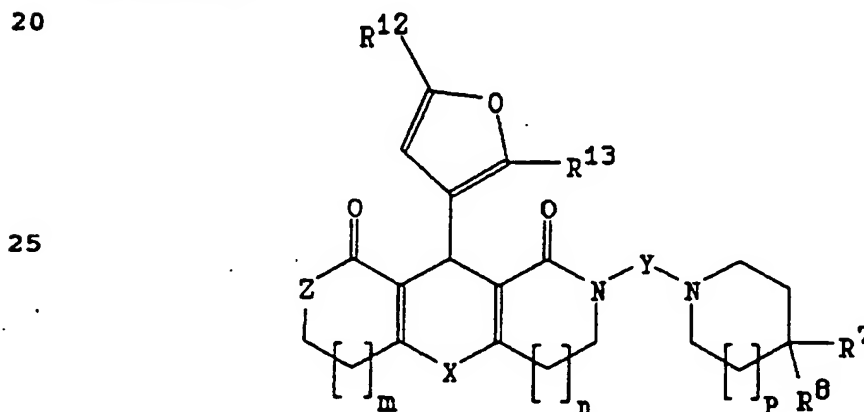
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quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v ,
 OCONHR^v , NH_2 , NHR^v , NR^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where
 R^v is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R^{12} and R^{13} are independently the same or
 15 different and are H or a linear chain alkyl group; and
 wherein p is 0, 1, 2 or 3.

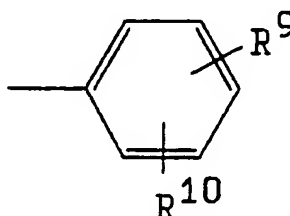
The invention further provides a compound having the
 structure:



30 wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-$
 $\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or
 different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the
 same or different and are 1, 2, 3 or 4; wherein Z is O,
 35 NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl
 or propyl group; wherein X is NH, NR' , O or S, where R'
 is H or a linear or branched chain alkyl or acyl group,

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or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO, COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a
 5 benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

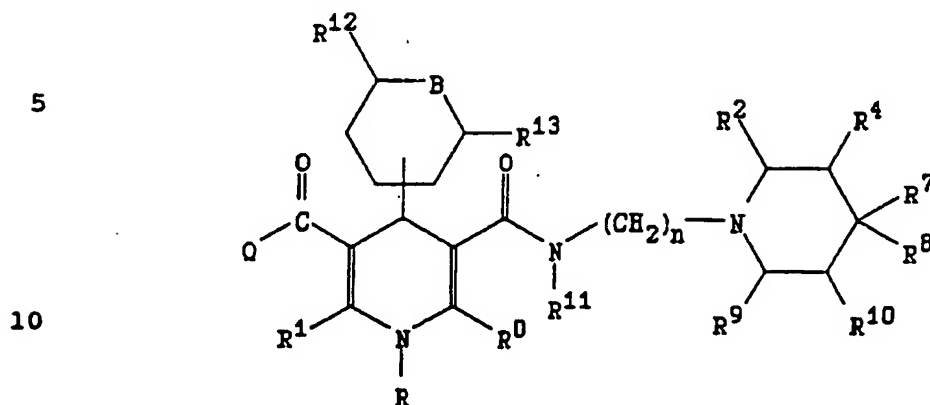


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is
 20 a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

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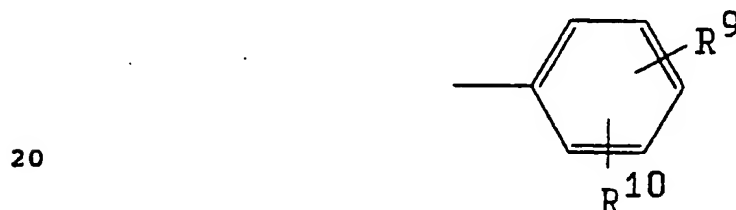
The invention still further provides a compound having the structure:



wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched chain alkyl group, or OH, OR^a, NH₂,
 15 NR^a, O(C=O)R^a or NH(C=O)R^a, where R^a is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein Q is OH, OR^{''}, SH, SR^{'''}, NH₂,
 NHR^{'''}, NR^{'''}, NR^{''}OH, NR^{''}OR^{'''}, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl
 20 or alkynyl group, or an aryl group, where R^{''} is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R^{'''} is a linear or branched chain alkyl group, or an aryl group; wherein R⁰
 and R¹ are independently the same or different and are H,
 25 a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR['], NR['], NHOH, N⁺R₃'Z⁻,
 NHCOR['], N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched
 30 chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R['] is a linear or branched chain alkyl group, or an aryl group, where W⁰
 is O, S or NH, where W¹ is NH₂, NHR['], NR['], NHOH, N⁺R₃'Z⁻, NHCOR['], N₃ or NO₂, and where R['] is a linear or branched
 35 chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a

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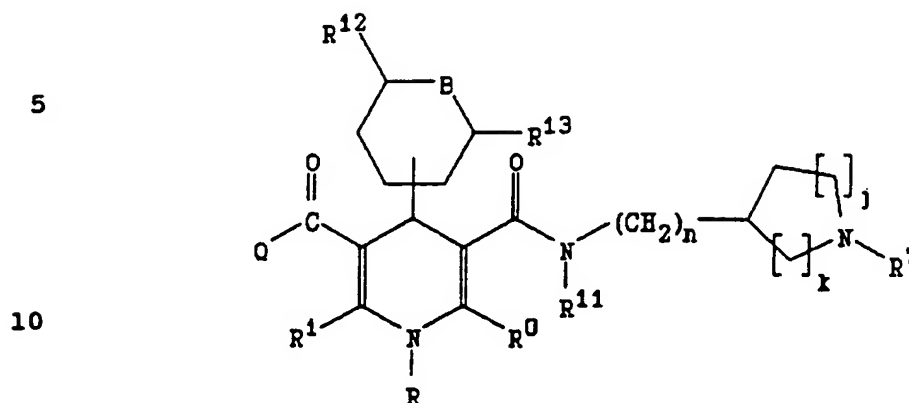
linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR'' , $OCOR''$, $OCOOR''$, $OCONHR''$, NH_2 , NHR'' , NR''_2 , $NHCOR''$, $NHCOOR''$ or $NHCONHR''$, where R' is a linear or branched chain alkyl group, and R'' is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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The invention also provides a compound having the structure:

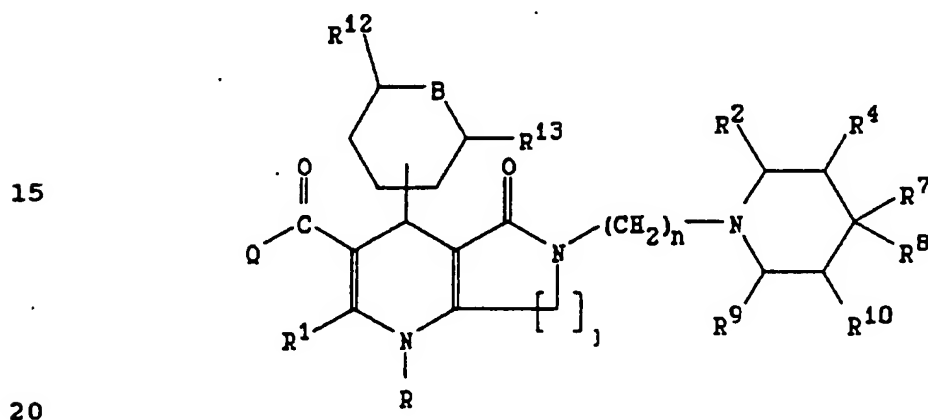


wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched chain alkyl group, or OH, OR^c, NH₂,
 15 NR₂^c, O(C=O)R^c or NH(C=O)R^c, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein Q is OH, OR^{''}, SH, SR^{'''}, NH₂, NHR^{'''},
 NR₂^{'''}, NR^{''}OH, NR^{''}OR^{'''}, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or
 20 alkynyl group, or an aryl group, where R^{''} is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R^{'''} is a linear or branched chain alkyl group, or an aryl group; wherein R⁰
 and R¹ are independently the same or different and are H,
 25 a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR['], NR₂['], NHOH, N⁺R₃[']Z⁻,
 NHCOR['], N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched
 30 chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R['] is a linear or branched chain alkyl group, or an aryl group, where W⁰
 is O, S or NH, where W¹ is NH₂, NHR['], NR₂['], NHOH, N⁺R₃[']Z⁻, NHCOR['], N₃ or NO₂, and where R['] is a linear or branched
 35 chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a

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linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 is an aryl or diarylalkyl group; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

The invention further provides a compound having the structure:

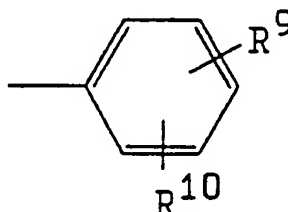


wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched chain alkyl group, or OH, OR^c, NH₂, NR^c, O(C=O)R^c or NH(C=O)R^c, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein Q is OH, OR^{''}, SH, SR^{'''}, NH₂, NHR^{'''}, NR₂^{'''}, NR^{''}OH, NR^{''}OR^{'''}, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R^{''} is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R^{'''} is a linear or branched chain alkyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_jW, where W is NH₂, NHR['], NR₂['], NHOH, N⁺R₃[']Z⁻, NHCOR['], N₃, NO₂ or CH₂W⁰(CH₂)_kW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl

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or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

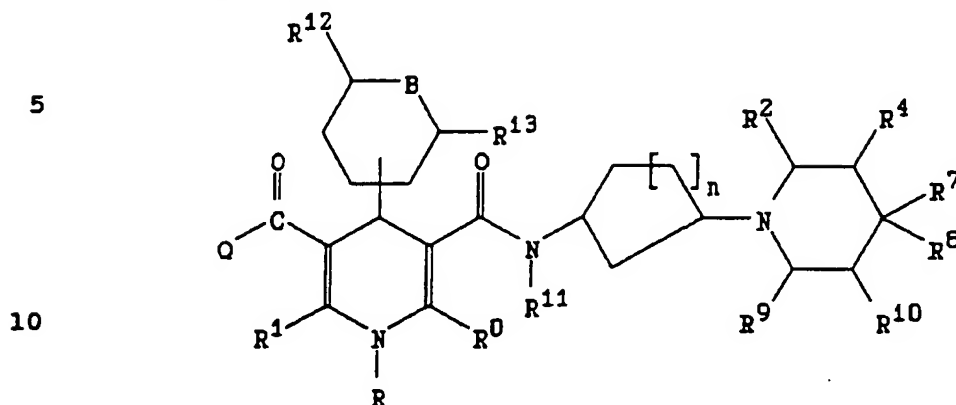
25



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR_2^v , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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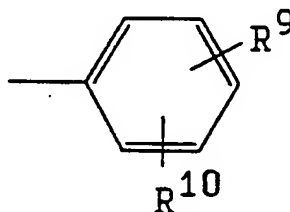
The invention still further provides a compound having the structure:



wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched chain alkyl group, or OH, OR^c, NH₂, NR^e, O(C=O)R^c or NH(C=O)R^c, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein Q is OH, OR^{''}, SH, SR^{'''}, NH₂, NHR^{'''}, NR₂^{'''}, NR^{''}OH, NR^{''}OR^{'''}, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R^{''} is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R^{'''} is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR['], NR₂['], NHOH, N⁺R₃[']Z⁻, NHCOR['], N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R['] is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR['], NR₂['], NHOH, N⁺R₃[']Z⁻, NHCOR['], N₃, or NO₂, and where R['] is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a

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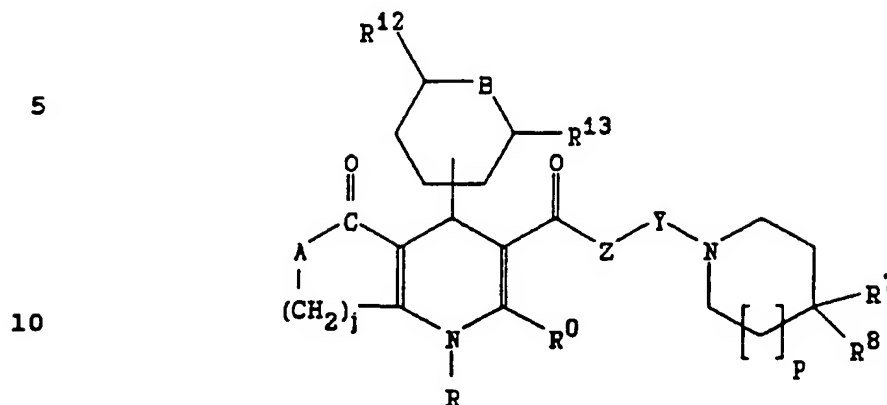
linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 0, 1, 2, 3 or 4.

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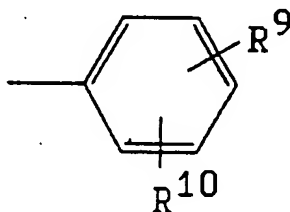
In addition, the invention provides a compound having the structure:



wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched chain alkyl group, or OH, OR^c, NH₂,
 15 NR₂, O(C=O)R^c or NH(C=O)R^c, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -
 20 (CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH₂, CR₂, NH, NR', NCHO, NCOR', NOH, O or S, where R' is a methyl, ethyl or propyl group; wherein Z is O, NH, NCHO, NCOR'', NR'', NOR'' or CH₂, where R'' is a methyl, ethyl
 25 or propyl group; wherein R is H or a linear or branched chain alkyl, or acyl group, or an aryl group; wherein R⁰ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl
 30 group, or (CH₂)_lW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_lW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰
 35 is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a

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pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; H, or a linear or branched chain, alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:

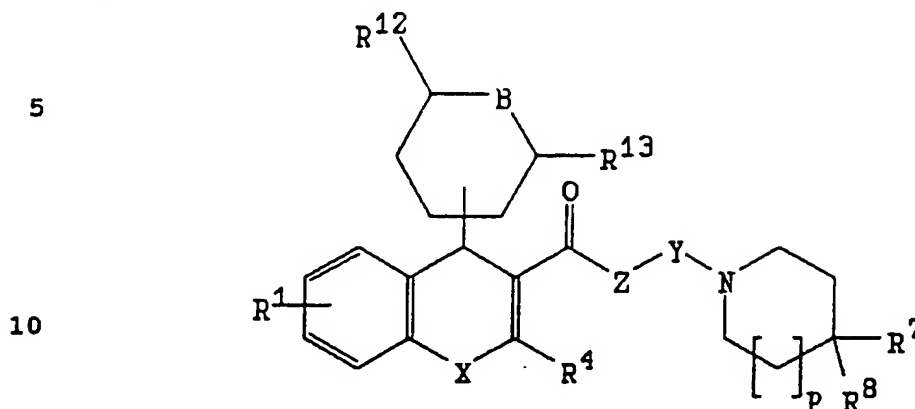


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

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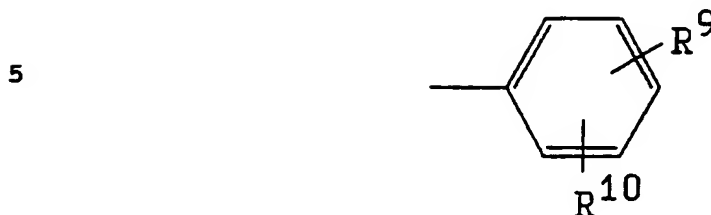
The invention also provides a compound having the structure:



wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched chain alkyl group, or OH, OR^c, NH₂,
 15 NR^c, O(C=O)R^c or NH(C=O)R^c, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein X is NH, NR['], O or S, where R['] is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5;
 20 -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR^{''}, NR^{''}, NOR^{''} or CH₂, where R^{''} is a
 25 methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, Cl, Br, I, F, NO₂, CN, OH, OR², OCOR², NH₂, NR², NHCOR₂ or CF₃, where R² is a linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, or a
 30 linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR['], OCOR['], NH₂, NHR['], NR['], NHCOR['], CONH₂, CONHR['], CONR₂['], COOH, COOR['], CHO, COR['], COSH, COSR['], COO(CH₂)₄OH or COO(CH₂)₄OR['], or a benzyl
 35 group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,

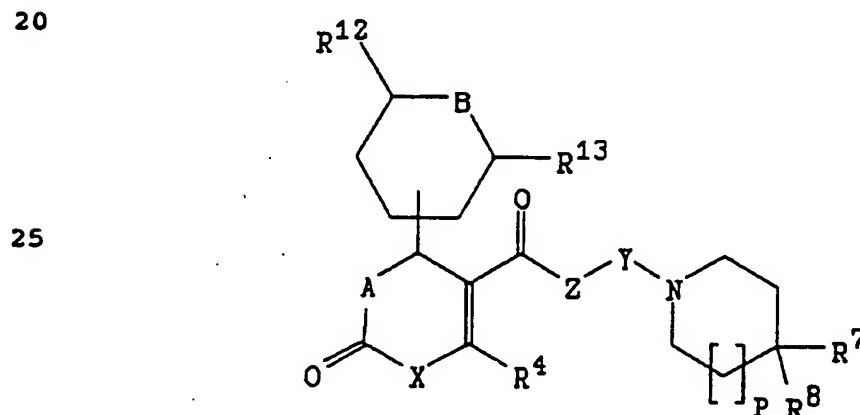
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furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
 OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where
 R^v is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R¹² and R¹³ are independently the same or
 15 different and are H or a linear chain alkyl group; and
 wherein p is 0, 1, 2 or 3.

The invention further provides a compound having the structure:

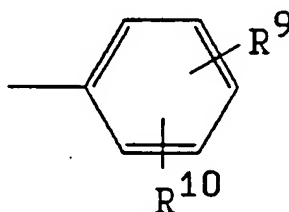


30 wherein A is CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S,
 where R is a methyl, ethyl or propyl group; B is O, S,
 CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched
 chain alkyl group, or OH, OR^c, NH₂, NR^c₂, O(C=O)R^c or
 NH(C=O)R^c, where R^c is H or a linear alkyl group, and
 35 where R^b is a linear or branched chain alkyl group;
 wherein X is NH, NR['], O or S, where R['] is H or a linear
 or branched chain alkyl or acyl group, or an aryl group;

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wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-$
 $O-(CH_2)_k-$, where h and k are independently the same or
different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the
5 same or different and are 1, 2, 3 or 4; wherein Z is O,
NH, NCHO, NCOR'', NR'', NOR'' or CH₂, where R'' is a
methyl, ethyl or propyl group; wherein R⁴ is H, or a
linear or branched chain alkyl group, or an aryl group;
wherein R⁷ and R⁸ are independently the same or different
10 and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂,
NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR',
COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl
group, a linear or branched chain alkyl or cycloalkyl
group, or are a heteroaryl group comprising a pyridyl,
15 indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,
furyl or thiophene group, or an aryl group having the
structure:

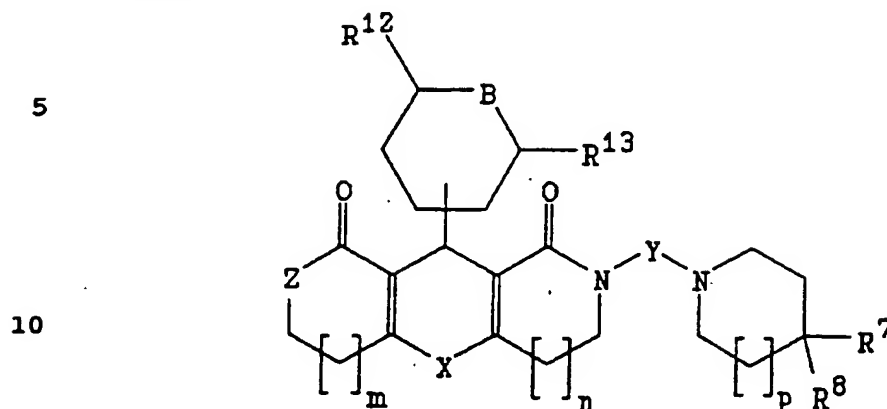
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wherein R⁹ and R¹⁰ are independently the same or different
25 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where
R' is a linear or branched chain alkyl group, and R^v is
a linear or branched chain alkyl group, and q is 2, 3, 4
or 5; wherein R¹² and R¹³ are independently the same or
30 different and are H or a linear chain alkyl group; and
wherein p is 0, 1, 2 or 3.

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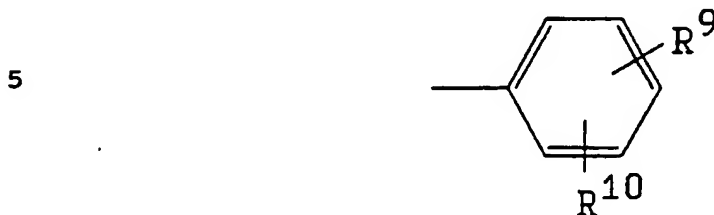
The invention further provides a compound having the structure:



wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched chain alkyl group, or OH, OR^c, NH₂,
 15 NR^c, O(C=O)R^c or NH(C=O)R^c, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein X is NH, NR', O or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5;
 20 -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR'', NR'', NOR'' or CH₂, where R'' is a
 25 methyl, ethyl or propyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)₄OH or COO(CH₂)₄OR', or a benzyl group, a linear or branched
 30 chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,

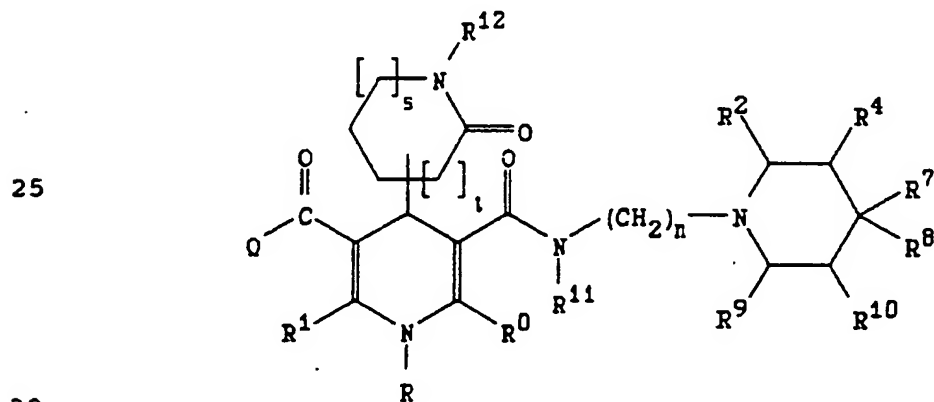
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quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
 OCONHR^v, NH₂, NHR^v, NR^v, NHCOR^v, NHCOOR^v or NHCONHR^v, where
 R' is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R¹² and R¹³ are independently the same or
 15 different and are H or a linear chain alkyl group;
 wherein m and n are independently the same or different
 and are 0 or 1; and wherein p is 0, 1, 2 or 3.

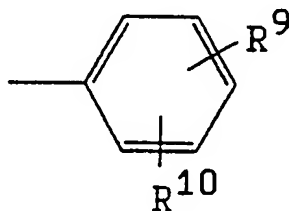
The invention still further provides a compound having
 20 the structure:



wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR'',
 NR''OH, NR''OR'', or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl
 group, or an aryl group, where R'' is H, a linear or
 35 branched chain alkyl group, trialkylsilylalkyl,
 cyanoalkyl, or an aryl group, and R''' is a linear or
 branched chain alkyl group, or an aryl group; wherein R⁰

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and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2 W^0 (CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_q OH$ or $COO(CH_2)_q OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

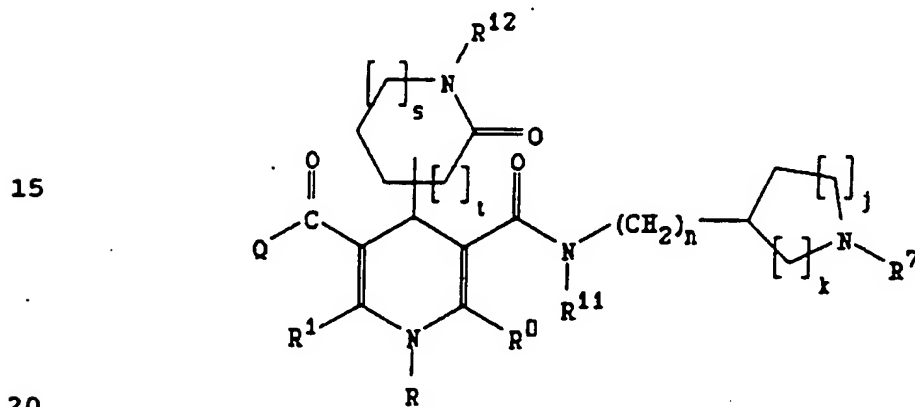


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^w , $OCOR^w$, $OCOOR^w$,

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OCONHR^v, NH₂, NHR^v, NR₂^v, NHCOR^v, NHCOOR^v or NHCONHR^v, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹¹ is H or a linear chain alkyl group;
 5 wherein R¹² is H or a linear chain alkyl group; wherein n is 2, 3 or 4; and wherein s and t are independently the same or different and are 0, 1, 2 or 3.

The invention also provides a compound having the
 10 structure:



wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR₂'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_lW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_lW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻,

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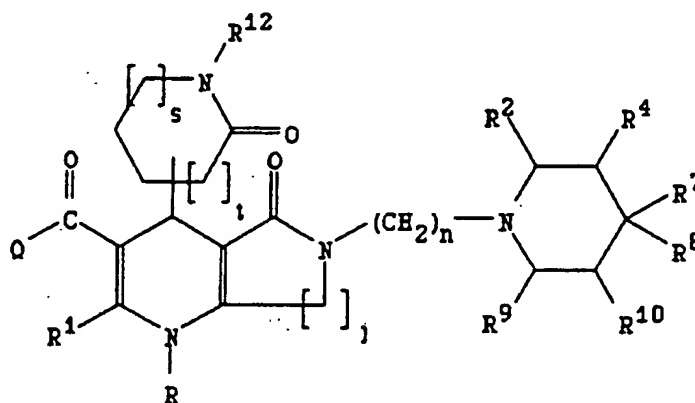
-193-

NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a
 5 linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁷ is an aryl or diarylalkyl group; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4;
 10 wherein n is 2, 3 or 4; and wherein s and t are independently the same or different and are 0, 1, 2 or 3.

The invention further provides a compound having the structure:

15

20



25 wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or
 30 branched chain alkyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl
 35 group, or (CH₂)_nW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_nW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl

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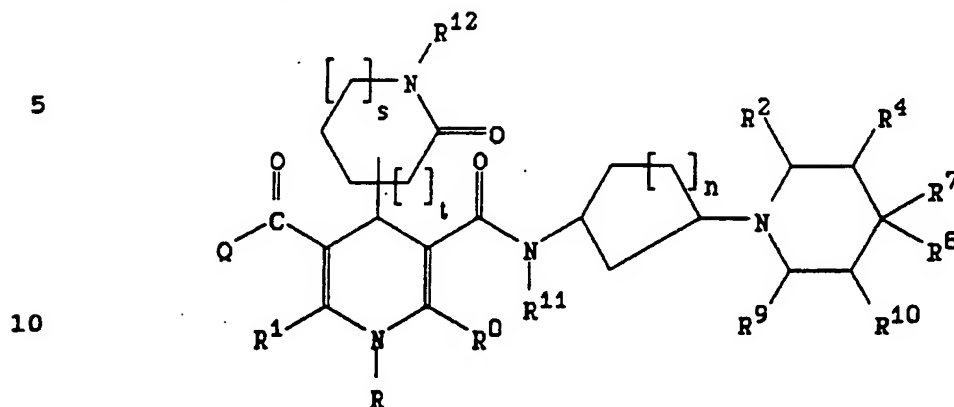
or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR_2^v , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; wherein n is 2, 3 or 4; and wherein s and t are independently the same or different and are 0, 1, 2 or 3.

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The invention still further provides a compound having the structure:

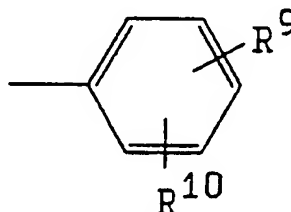


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_vW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain

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alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 ,
 5 OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,
 10 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

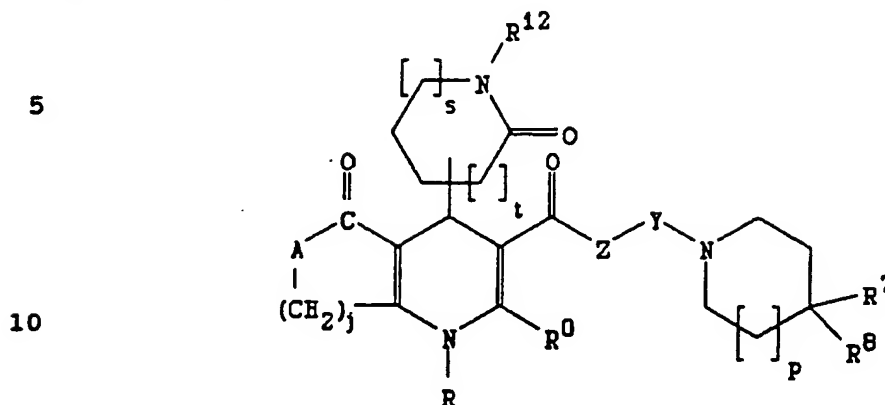
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$,
 20 $CONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; wherein j
 25 is 1, 2, 3 or 4; wherein n is 0, 1, 2, 3 or 4; and wherein s and t are independently the same or different and are 0, 1, 2 or 3.

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The invention also provides a compound having the structure:



wherein Q is OH, OR', SH, SR'', NH₂, NHR'', NR'OH, NR'OR'', where R' is H, or a linear or branched chain alkyl, trialkylsilylalkyl, or cyanoalkyl group, or an aryl group, and where R'' is a linear or branched chain alkyl group, or an aryl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-, or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Z is O, NH, NCHO, NCOR^b, NR^b, NOR^b, or CH₂, where R^b is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ is H, or a linear or branched chain alkyl, alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, or hydroxyalkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR', NHCOR', CONH₂, CONHR', CONR', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl,

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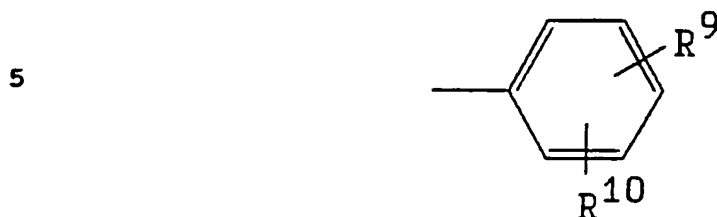
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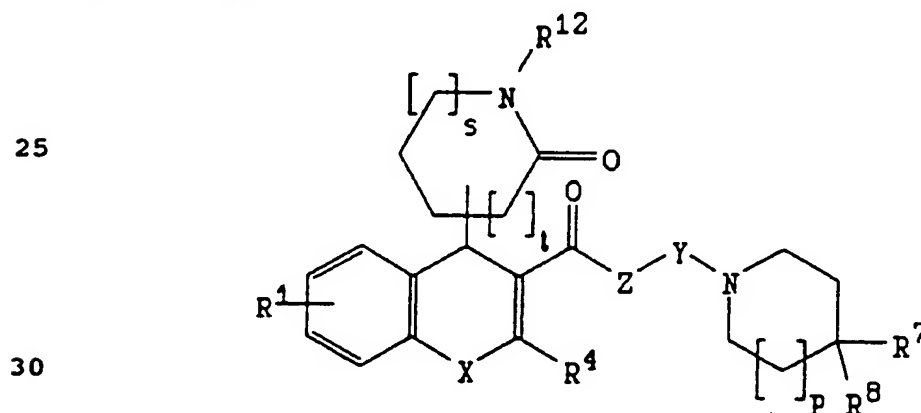
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indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^q , OCOR^q , OCOOR^q ,
 OCONHR^q , NH_2 , NHR^q , NR^q , NHCOR^q , NHCOOR^q or NHCONHR^q , where
 R^q is a linear or branched chain alkyl group, and R^q is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R^{12} is H or a linear chain alkyl group;
 15 wherein j is 1, 2, 3 or 4; wherein p is 0, 1, 2 or 3; and
 wherein s and t are independently the same or different
 and are 0, 1, 2 or 3.

20 The invention further provides a compound having the
 structure:



wherein X is NH, NR, O or S, where R is H or a linear or
 branched chain alkyl or acyl group, or an aryl group; Y
 is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$
 35 -, where h and k are independently the same or different
 and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-$
 $(\text{CH}_2)_k-$, where h and k are independently the same or

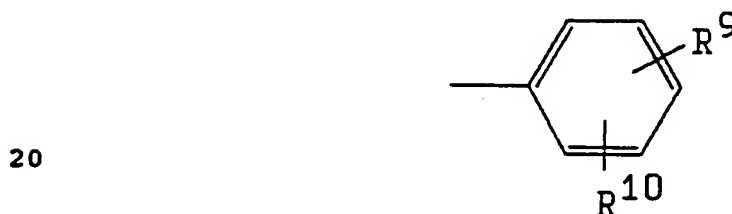
-199-

different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein R¹ is H, Cl, Br, I, F, NO₂, CN, OH, OR'', OCOR'', NH₂, NR'', NHCOR'' or CF₃, where R'' is a

5 linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR', NHCOR', CONH₂, CONHR', CONR₂',

10 COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

15 group, or an aryl group having the structure:



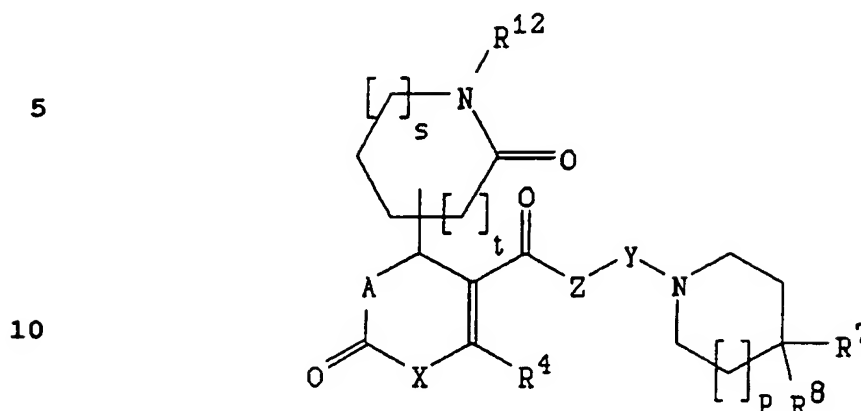
wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v, OCONHR^v, NH₂, NHR^v, NR^v, NHCOR^v, NHCOOR^v or NHCONHR^v, where

25 R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein p is 0, 1, 2 or 3; and wherein s and t are independently the same or different

30 and are 0, 1, 2 or 3.

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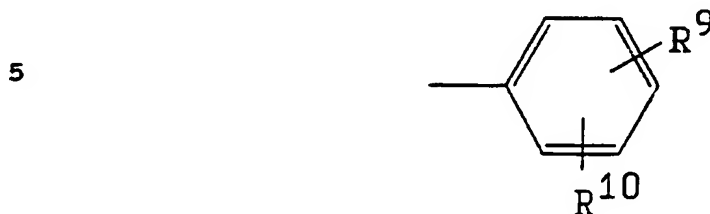
The invention also provides a compound having the structure:



- wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S ,
 15 where R is a methyl, ethyl or propyl group; wherein X is NH , NR' , O or S , where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and
 20 are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR'' , NR'' , NOR'' or CH_2 , where R'' is a methyl, ethyl or propyl group; wherein R' is H , or a linear or branched chain
 25 alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H , CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched
 30 chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,

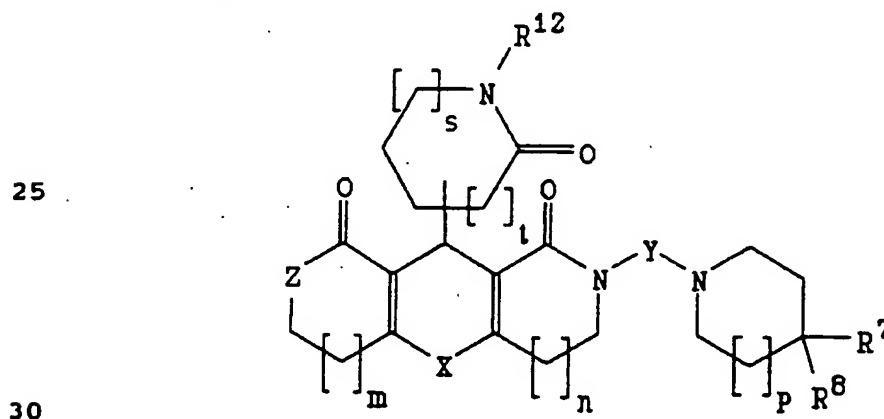
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quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
 OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where
 R' is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R¹² is H or a linear chain alkyl group;
 15 wherein j is 1, 2, 3 or 4; wherein p is 0, 1, 2 or 3; and
 wherein s and t are independently the same or different
 and are 0, 1, 2 or 3.

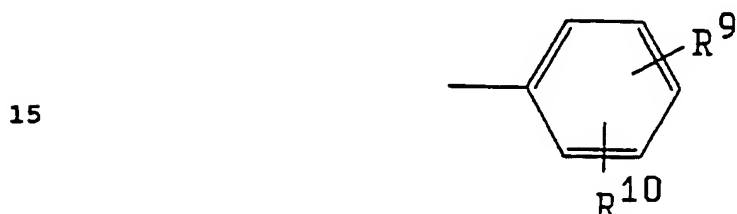
The invention also provides a compound having the
 20 structure:



wherein X is NH, NR, O or S, where R is H or a linear or
 branched chain alkyl or acyl group, or an aryl group; Y
 is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-,
 35 where h and k are independently the same or different and
 are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-,
 where h and k are independently the same or different and

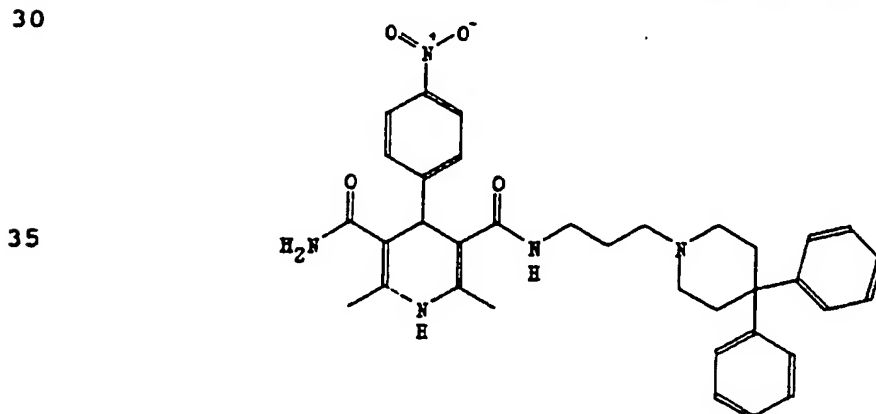
-202-

are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂,
 5 NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,
 10 furyl or thiophene group, or an aryl group having the structure:



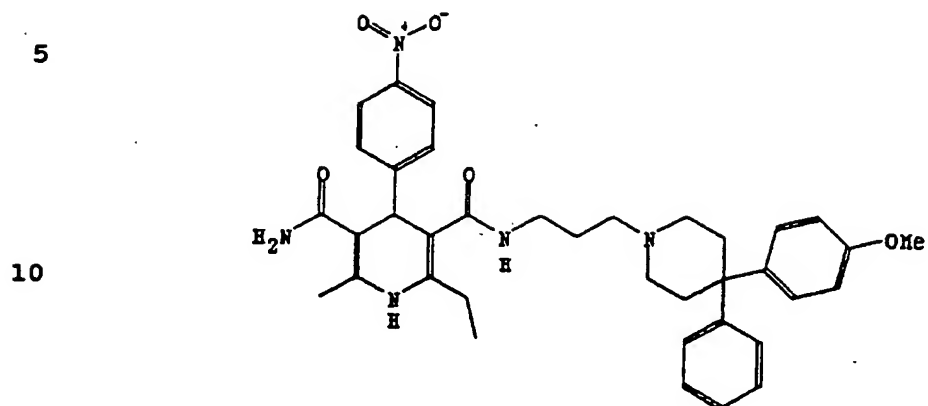
wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
 20 OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein m and n are
 25 independently the same or different and are 0 or 1; wherein p is 0, 1, 2 or 3; and wherein s and t are independently the same or different and are 0, 1, 2 or 3.

The invention provides a compound having the structure:

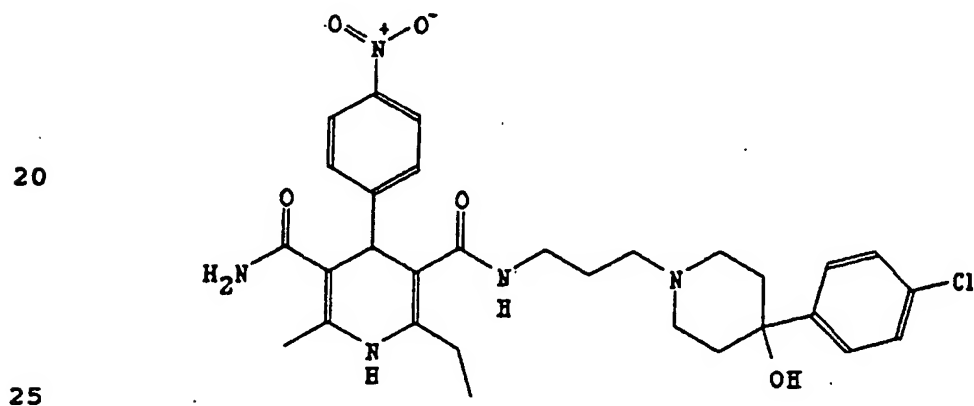


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The invention also provides a compound having the structure:

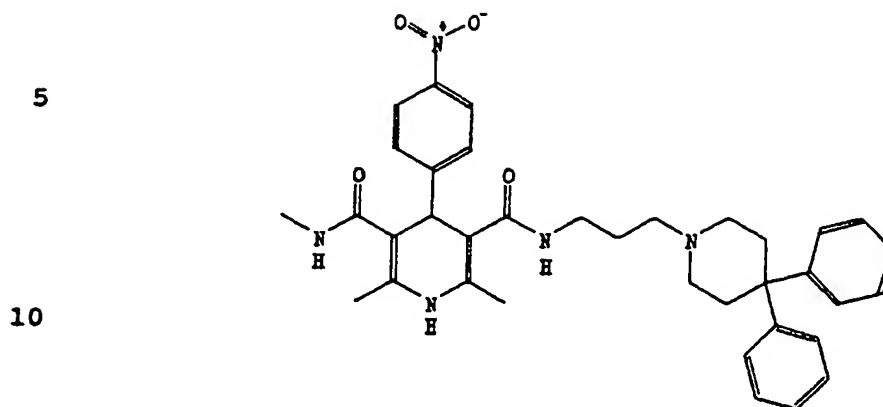


15 The invention further provides a compound having the structure:

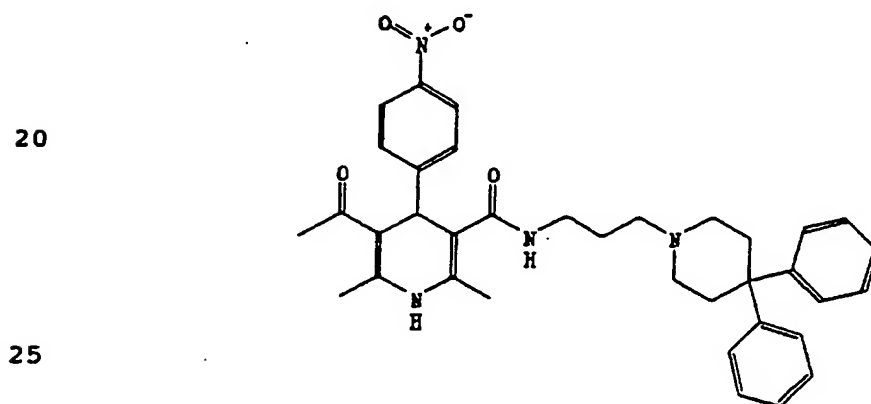


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The invention also provides a compound having the structure:

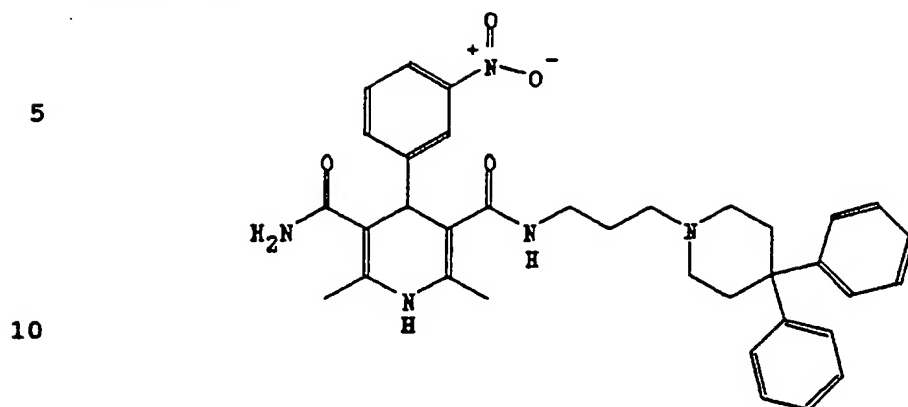


15 The invention further provides a compound having the structure:

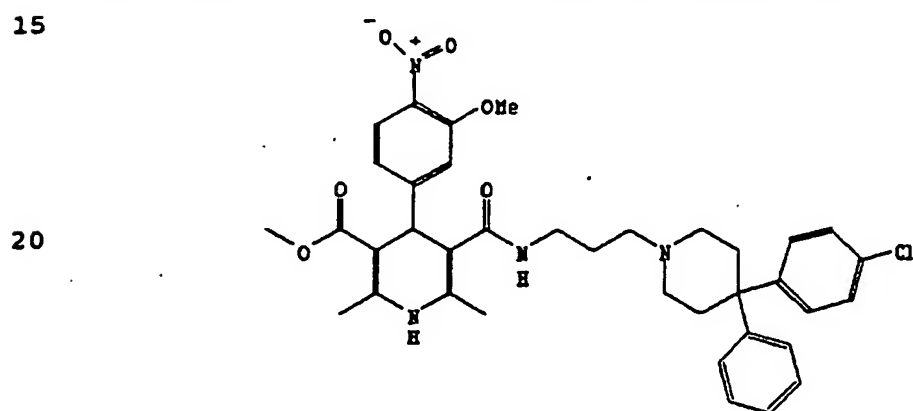


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The invention also provides a compound having the structure:

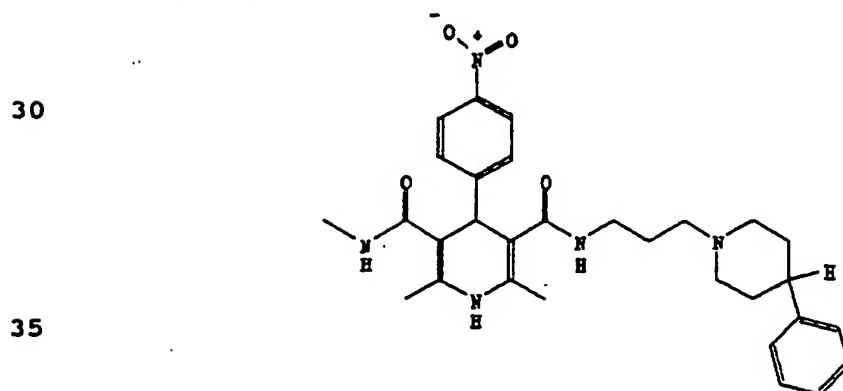


The invention provides a compound having the structure:



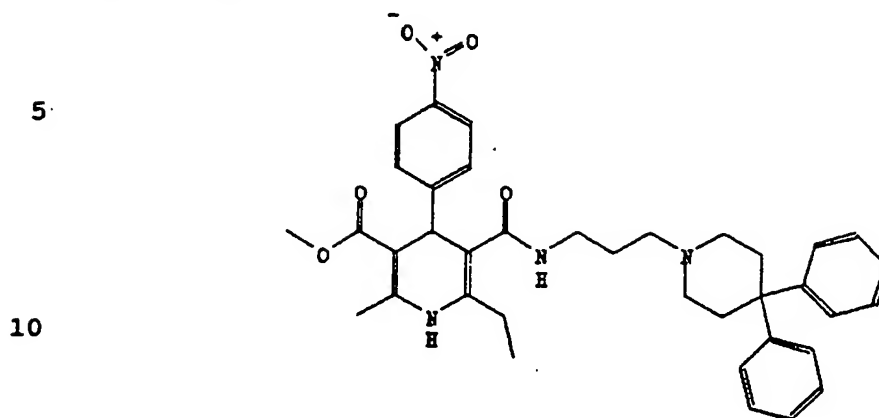
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The invention further provides a compound having the structure:

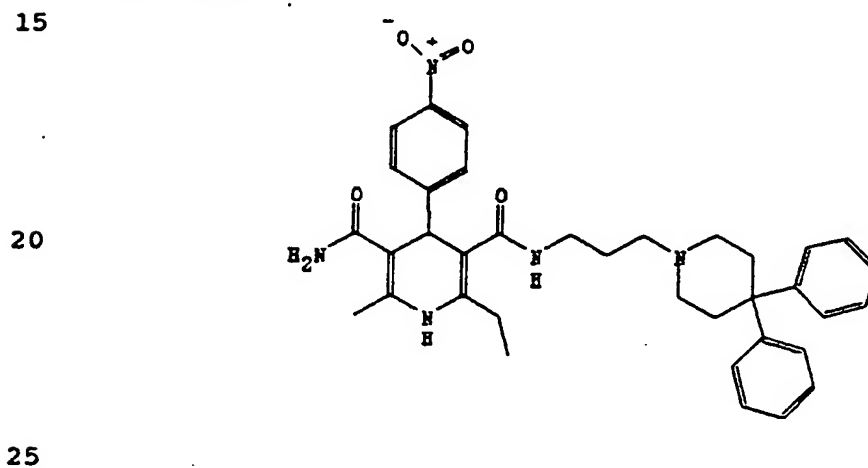


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The invention additionally provides a compound having the structure:

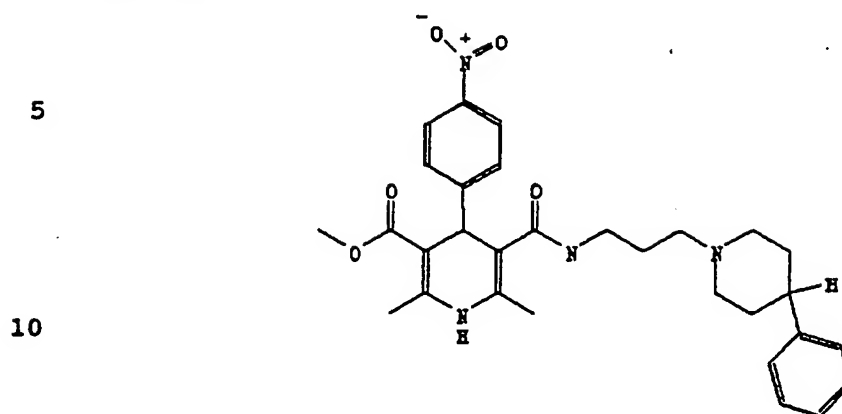


The invention further provides a compound having the structure:

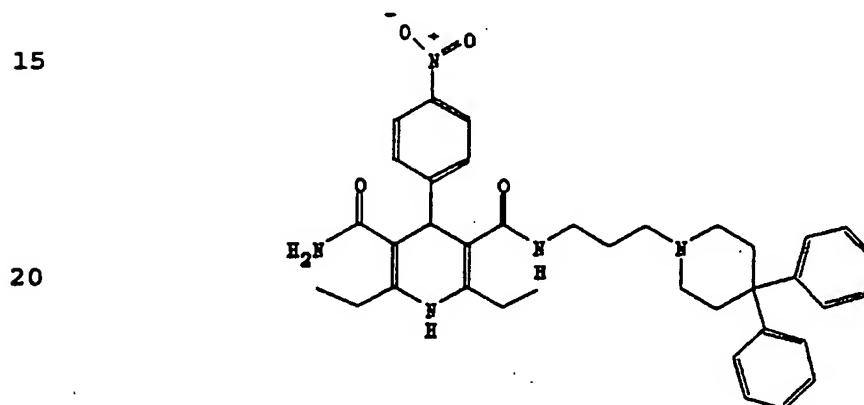


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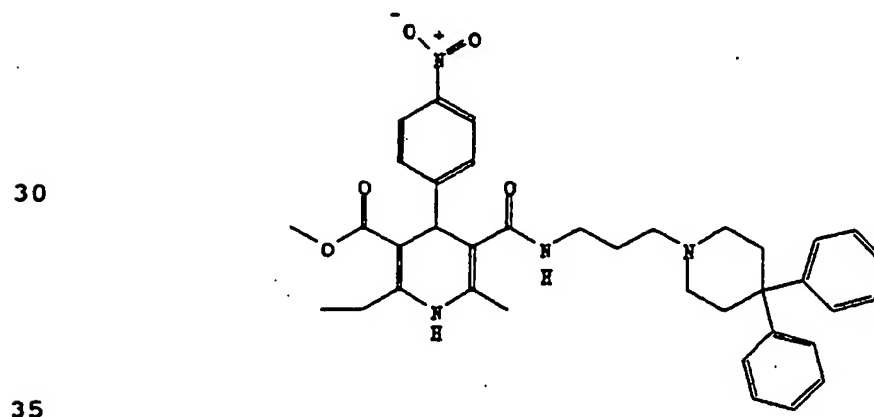
The invention also provides a compound having the structure:



The invention provides a compound having the structure:

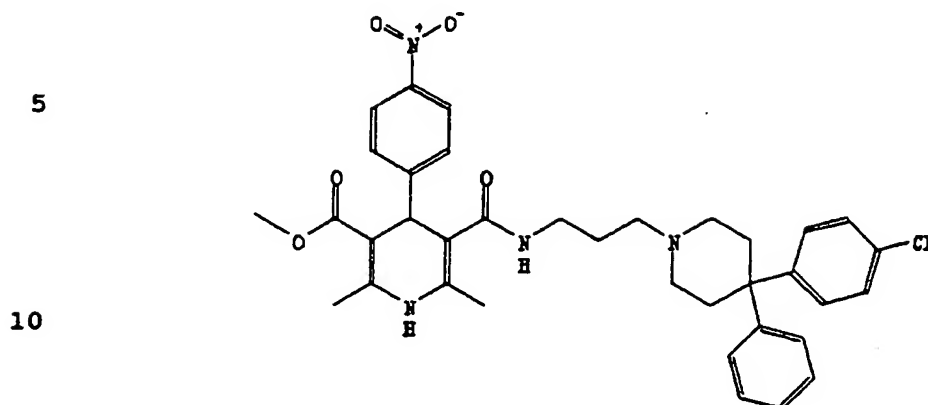


The invention also provides a compound having the structure:

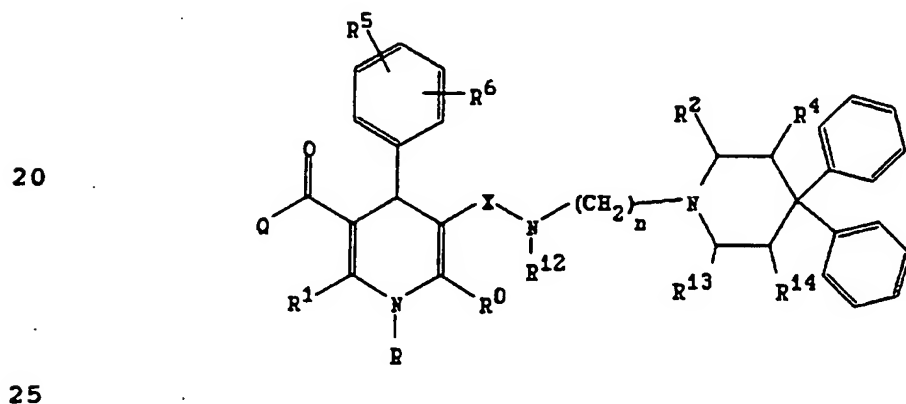


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The invention further provides a compound having the structure:



The invention also provides a compound having the structure:



30 wherein X is C=O, CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Q is OH, OR^{''}, SH, SR^{'''}, NH₂, NHR^{'''}, NR₂^{'''}, NR^{''}OH, NR^{''}OR^{'''}, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an

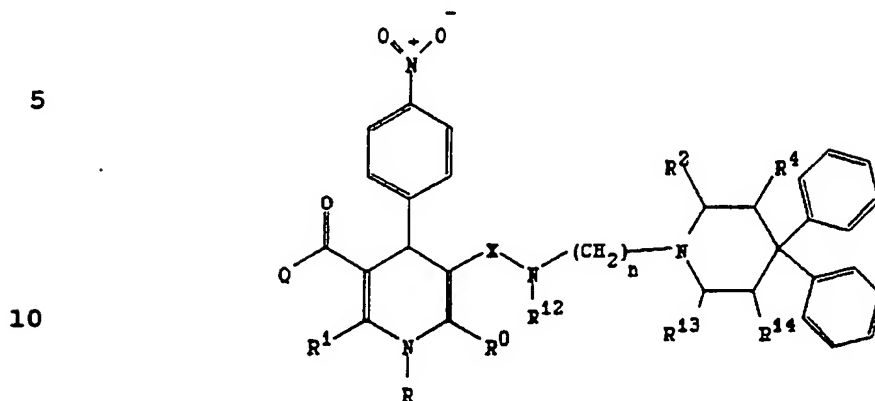
35 aryl group, where R^{''} is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R^{'''} is a linear or branched chain alkyl

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group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2 W^0 (CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^3 , and R^4 are independently the same or different and are H, or a linear or branched chain alkyl, hydroxyalkyl, alkoxyalkyl, amino alkyl or aryl group; wherein R^4 is a linear or branched chain alkyl, alkoxyalkyl, hydroxyalkyl or a linear or branched chain alkenylalkyl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, N_3 , NH_2 , CF_3 , a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^{12} is H or a linear chain alkyl group; and

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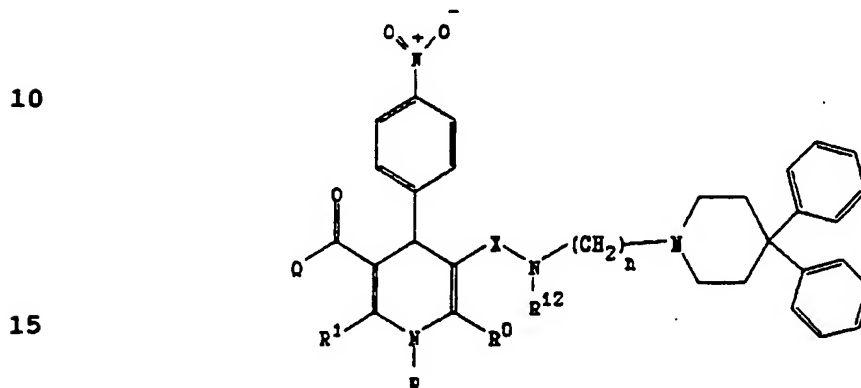
wherein n is 2, 3 or 4. In one embodiment, the invention provides a compound having the structure:



- 15 wherein X is C=O, CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R², R¹³, and R¹⁴ are independently the same or different and are H, or a linear or

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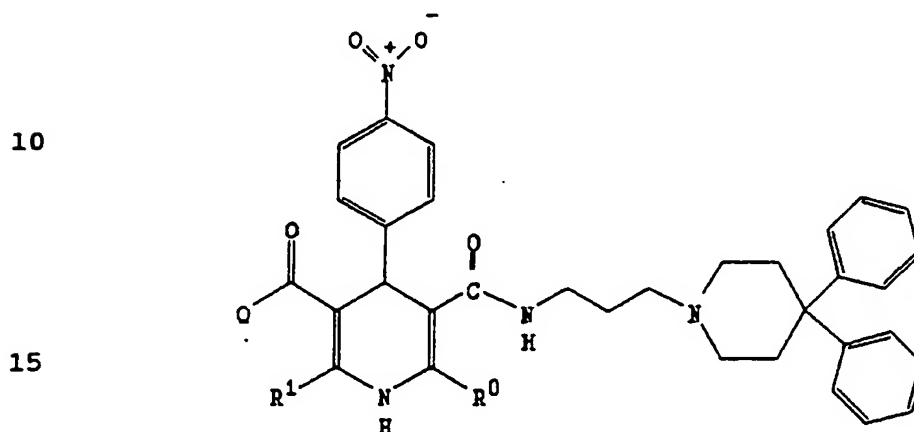
branched chain alkyl, hydroxyalkyl, alkoxyalkyl, amino alkyl or aryl group; wherein R^4 is a linear or branched chain alkyl, alkoxyalkyl, hydroxyalkyl or a linear or branched chain alkenylalkyl group; wherein R^{12} is H or a
 5 linear chain alkyl group; and wherein n is 2, 3 or 4. In another embodiment, the invention provides a compound having the structure:



wherein X is $C=O$, CH_2 , CR^a , NH , NR^a , $NCHO$, $NCOR^a$, NOH , O or S, where R^a is a methyl, ethyl or propyl group; wherein
 20 Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$ or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl
 25 group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl,
 30 aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched
 35 chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically

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acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹² is H or a linear chain alkyl group; and wherein n is 2, 3 or 4. In one embodiment, the invention provides a compound having the structure:

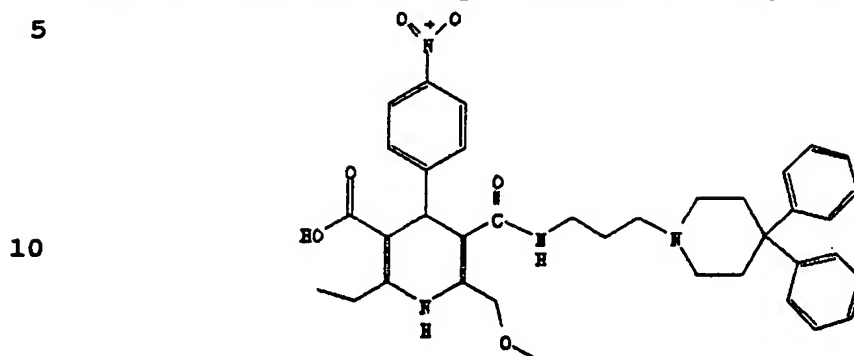


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; and wherein R is H,

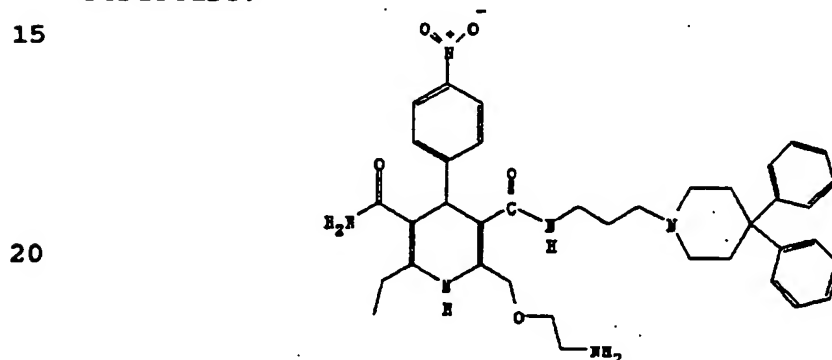
-213-

a linear or branched chain alkyl or acyl group, or an aryl group.

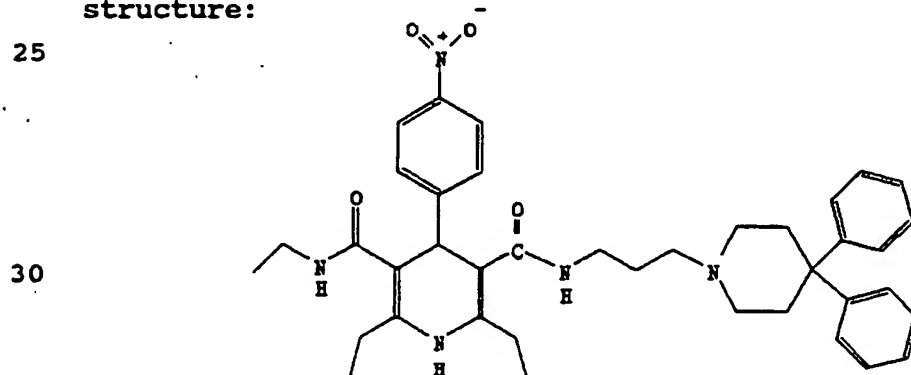
The invention provides a compound having the structure:



The invention also provides a compound having the structure:

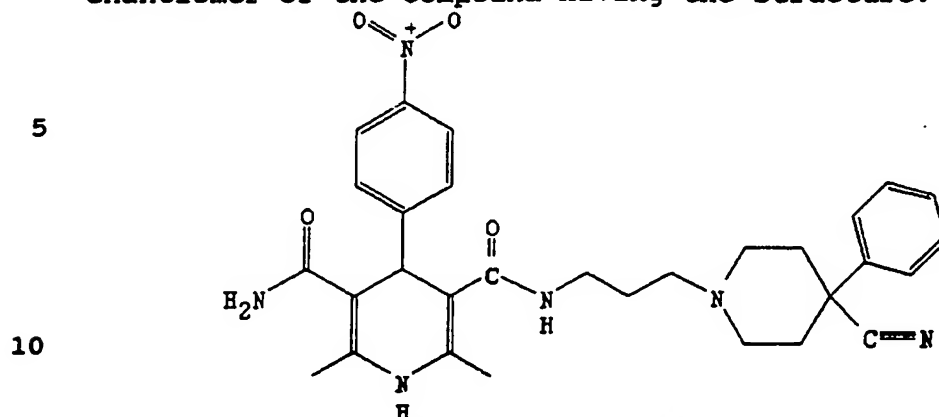


The invention further provides a compound having the structure:



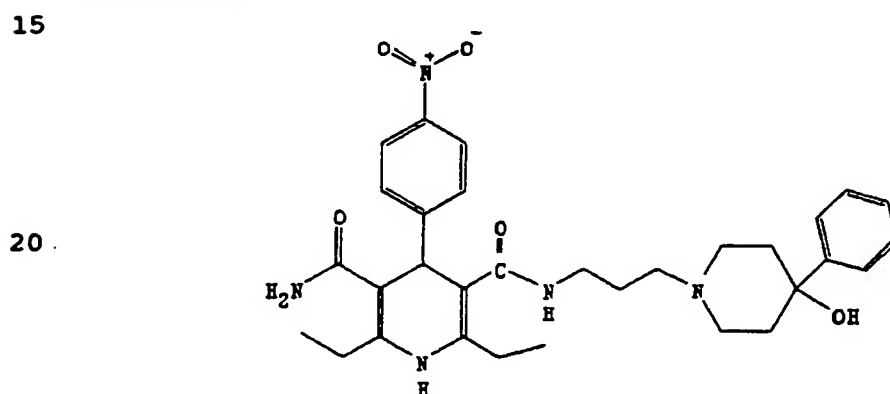
-214-

The invention still further provides the (+) and (-) enantiomer of the compound having the structure:



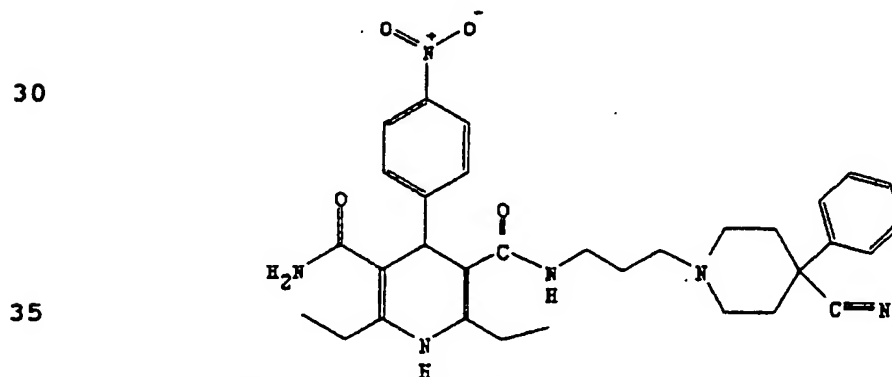
and pharmaceutically acceptable salts thereof.

The invention also provides a compound of having the structure:



25

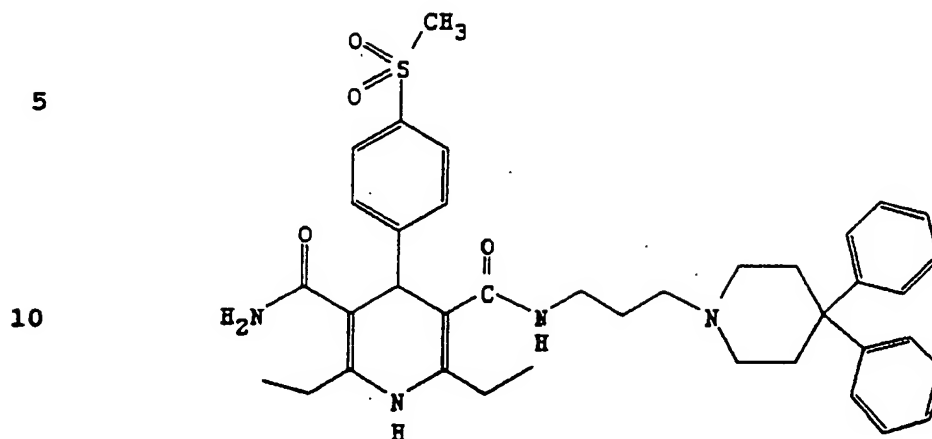
The invention additionally provides the (+) and (-) enantiomer of the compound having the structure:



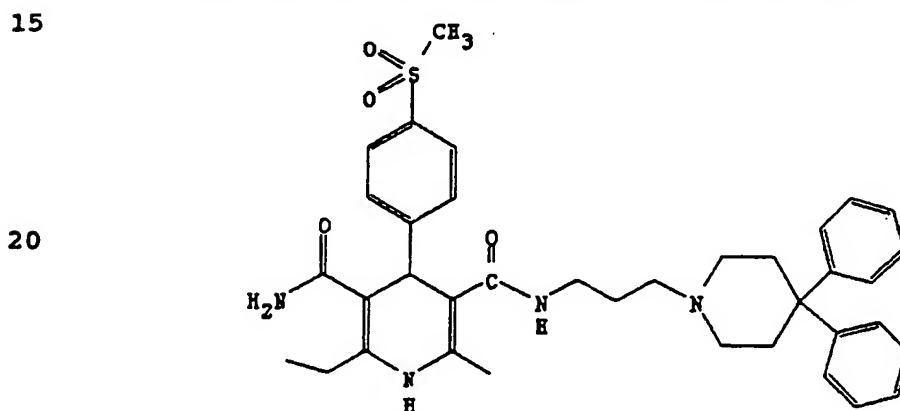
and pharmaceutically acceptable salts thereof.

-215-

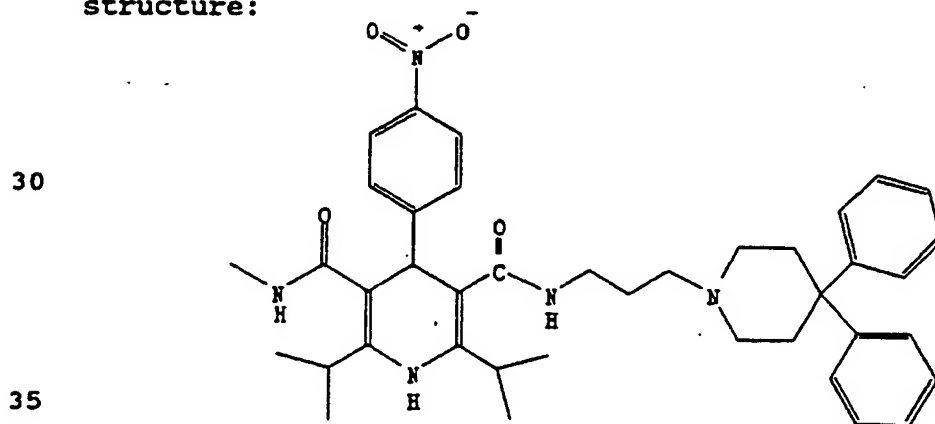
The invention also provides a compound having the structure:



The invention provides a compound having the structure:

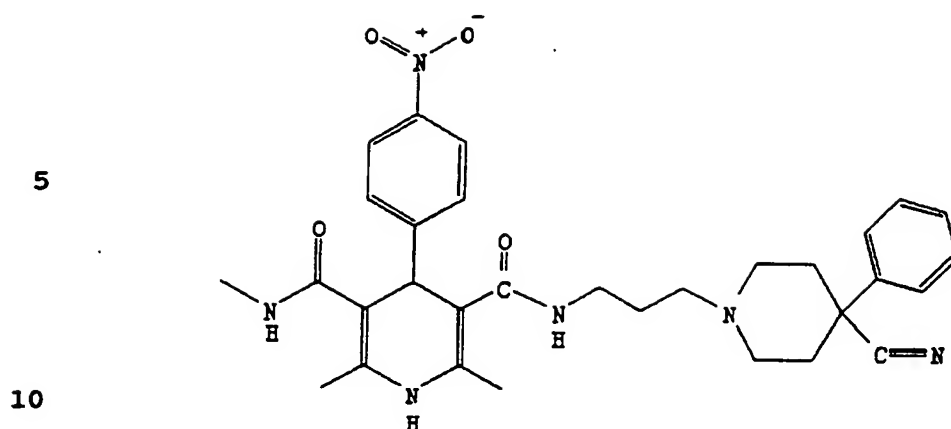


25 The invention also provides a compound having the structure:

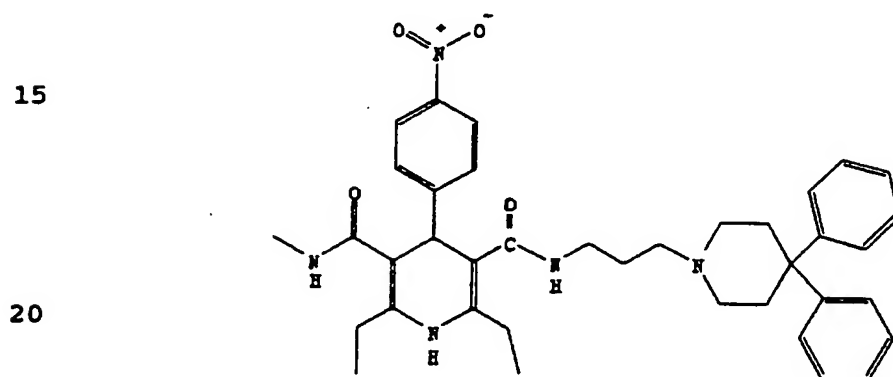


The invention additionally provides a compound having the structure:

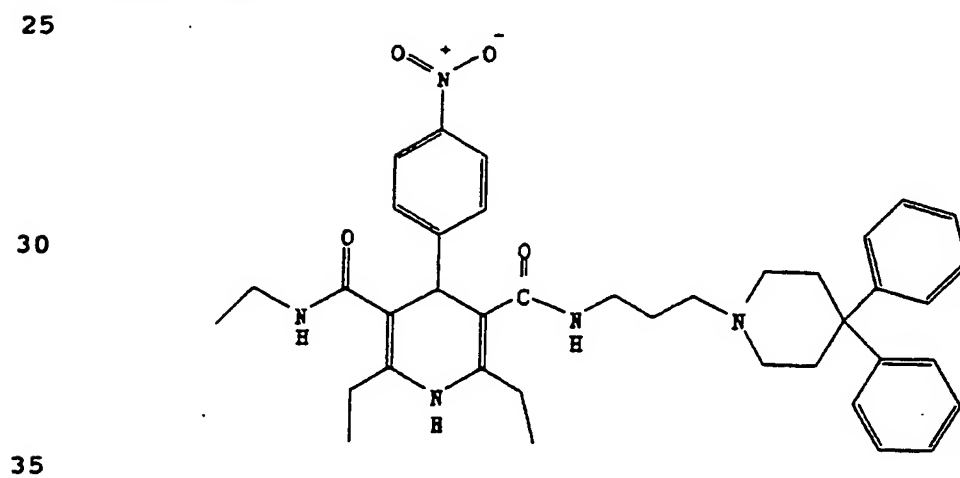
-216-



The invention provides a compound having the structure:

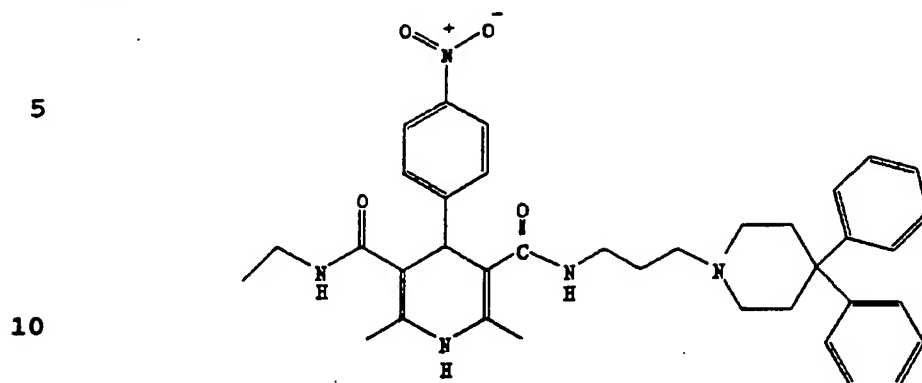


The invention also provides a compound having the structure:

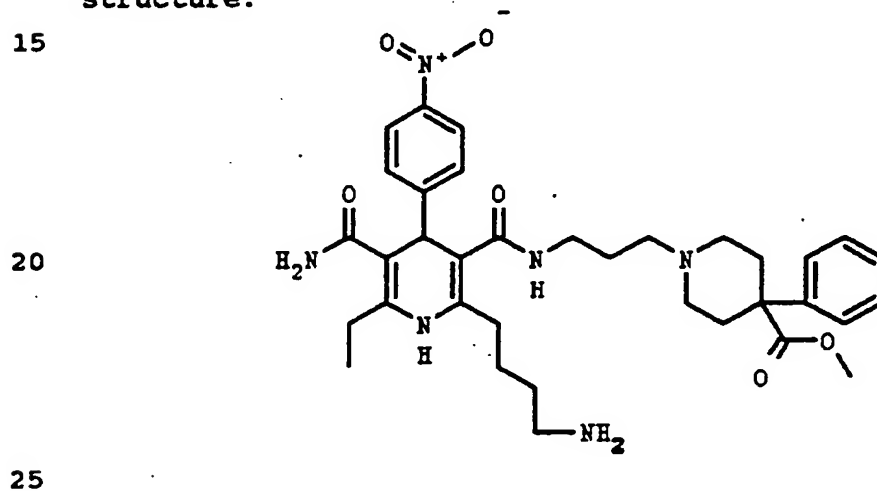


-217-

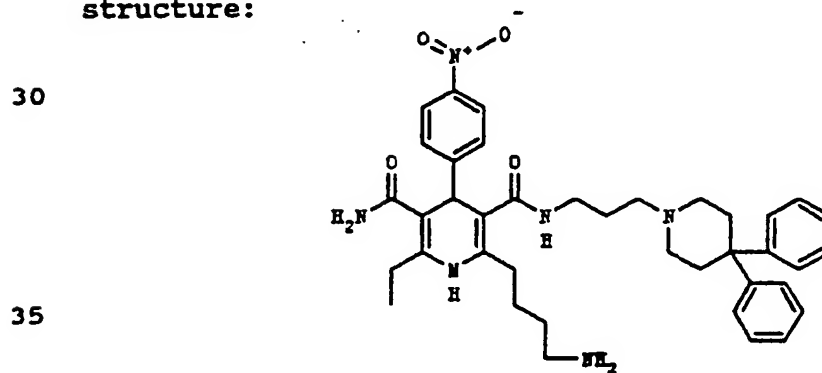
The invention further provides a compound having the structure:



The invention further provides a compound having the structure:

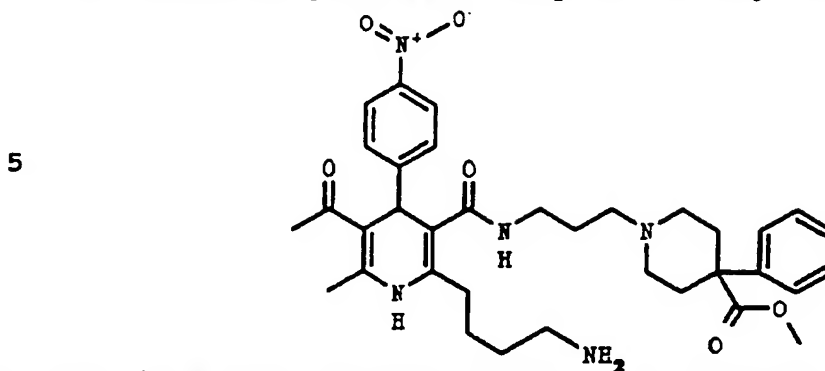


The invention also provides a compound having the structure:

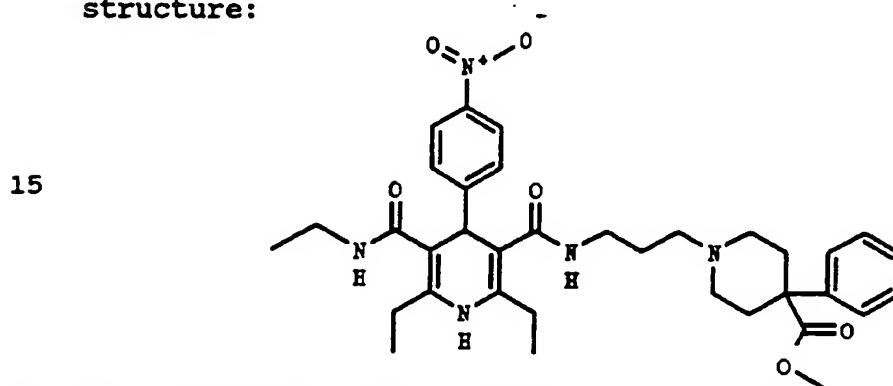


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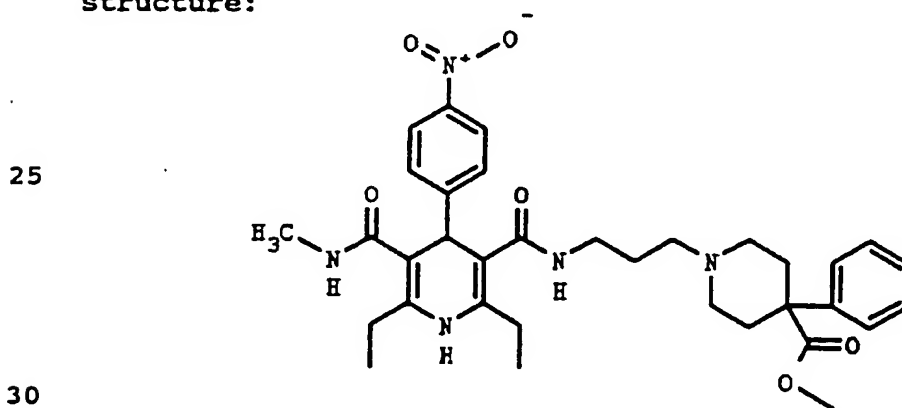
The invention provides a compound having the structure:



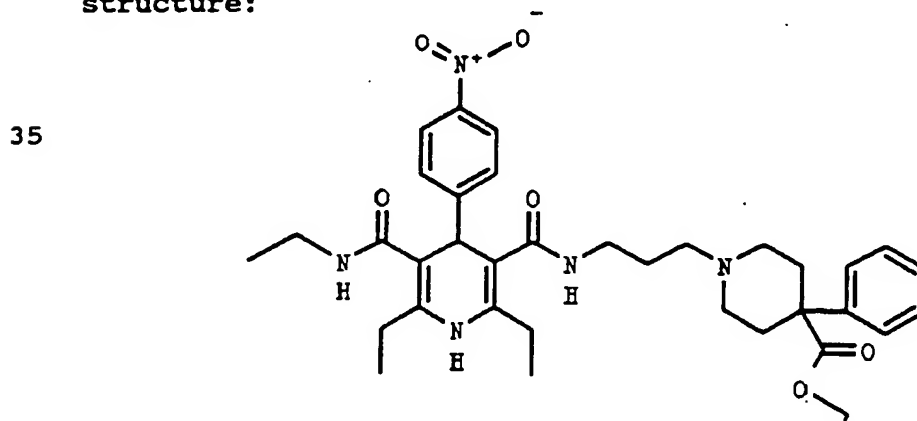
10 The invention further provides a compound having the structure:



20 The invention also provides a compound having the structure:

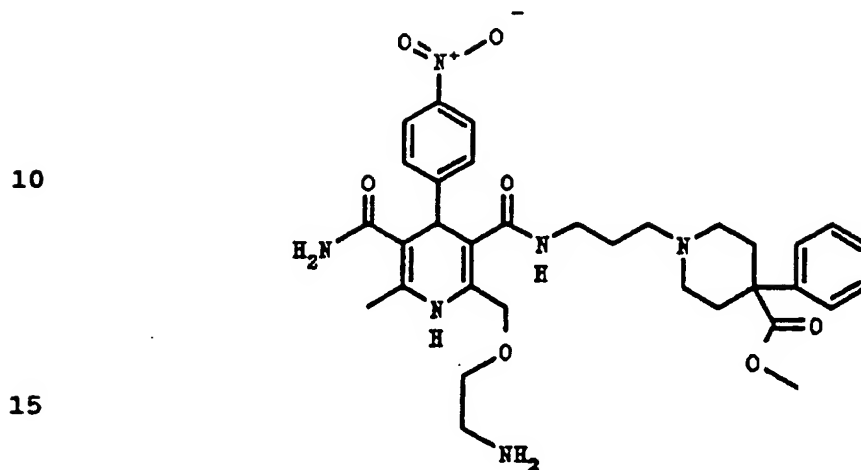


The invention further provides a compound having the structure:

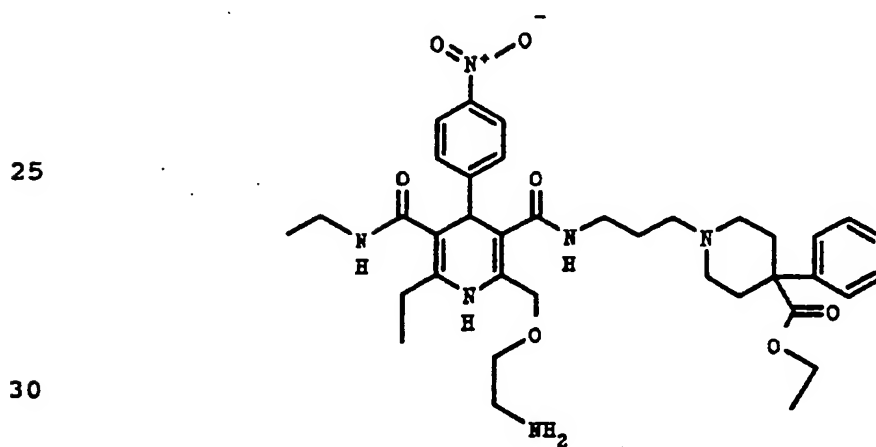


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The invention still further provides a compound having
5 the structure:

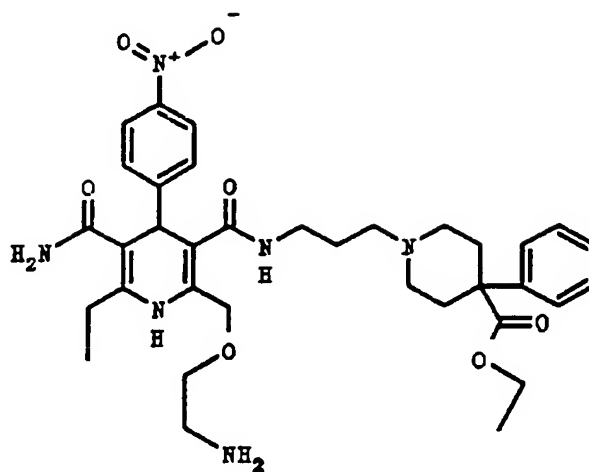


The invention also provides a compound having the
20 structure:



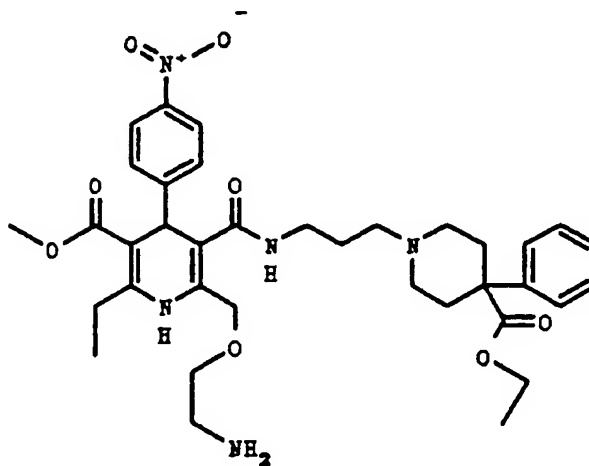
-220-

The invention further provides a compound having the structure:



15

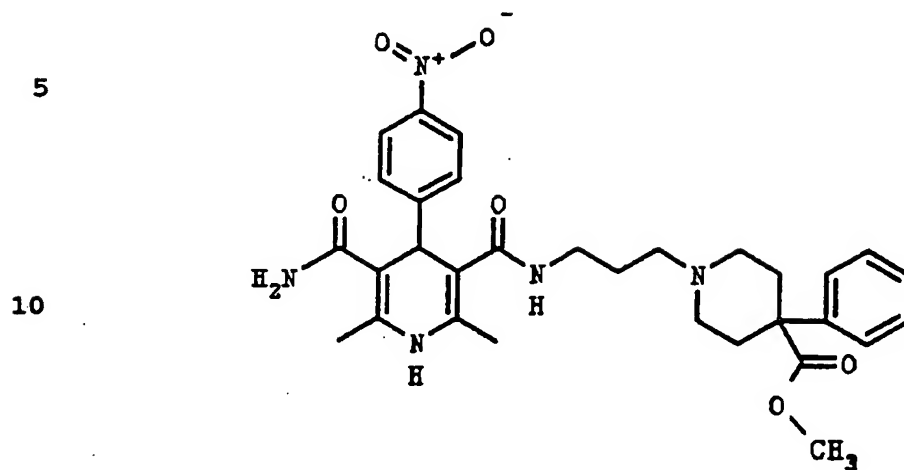
The invention also provides a compound having the structure:



30

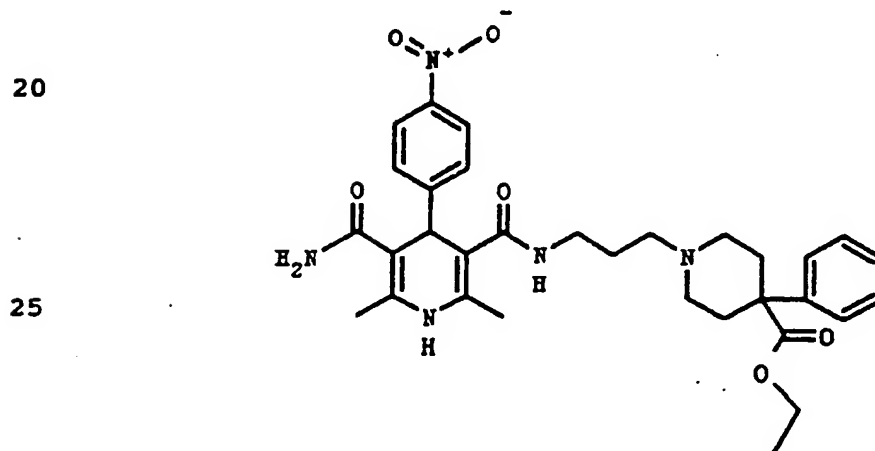
-221-

The invention further provides a compound having the structure:



15

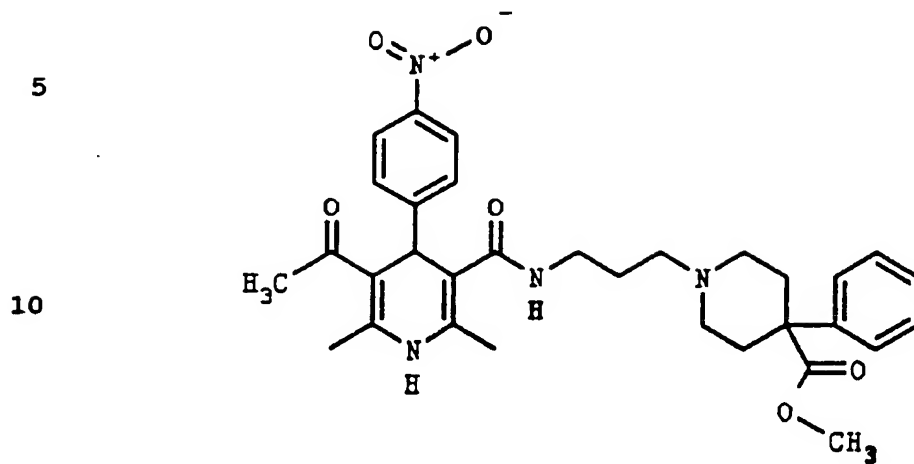
The invention still further provides a compound having the structure:



30

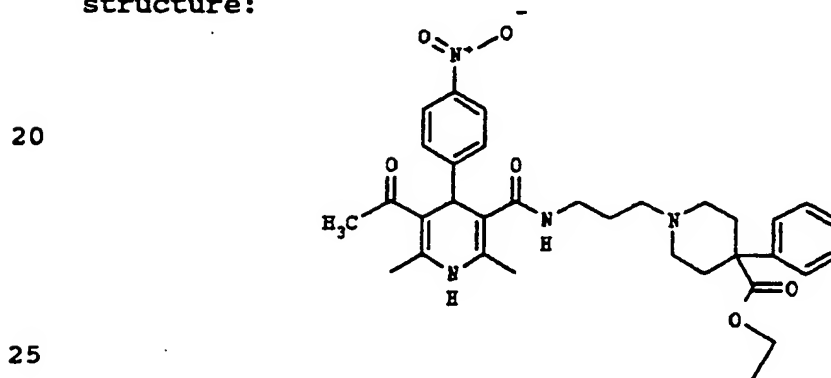
-222-

The invention also provides a compound having the structure:

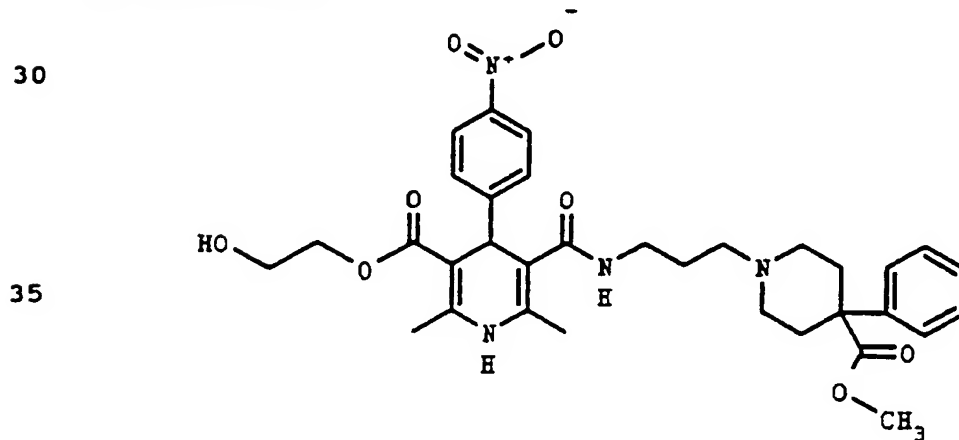


15

The invention further provides a compound having the structure:

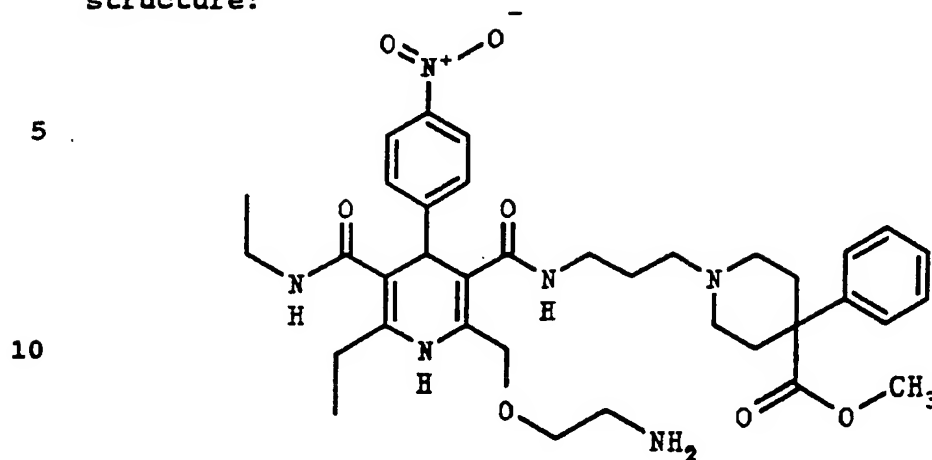


The invention still further provides a compound having the structure:



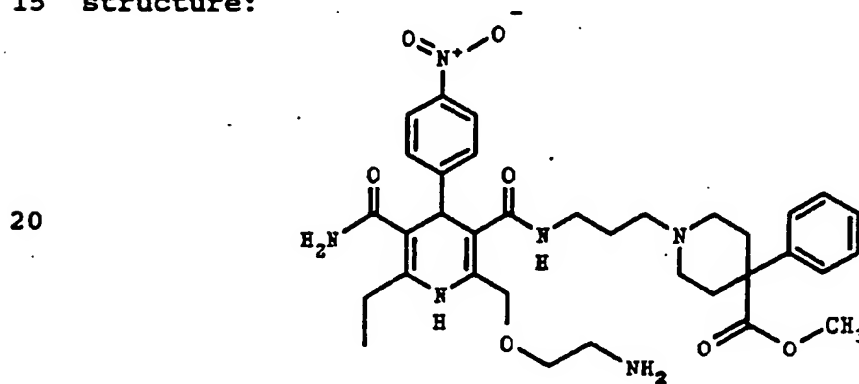
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The invention further provides a compound having the structure:



The invention also provides a compound having the structure:

15



25 The invention additionally provides a pharmaceutical composition which comprises the compound disclosed herein in a therapeutically effective amount and a pharmaceutically acceptable carrier. The invention includes the pharmaceutical composition wherein the carrier is a solid and the composition is a tablet. In such pharmaceutical compositions, the therapeutically effective amount is an amount from about 0.1 to about 500 mg. In certain embodiments, the therapeutically effective amount is from about 1 to 60 mg. The invention also includes a

30

35 pharmaceutical composition wherein the carrier is a liquid and the composition is a solution, wherein the therapeutically effective amount is an amount from about 0.1 to about 500 mg per mL of solution and in certain

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embodiments, the therapeutically effective amount is an amount from about 1 to about 60 mg per mL of solution. The invention further provides a pharmaceutical composition wherein the carrier is a gel and the composition
5 is a suppository, wherein the therapeutically effective amount is an amount from about 0.1 to about 500 mg.

The invention also encompasses a method of treating benign prostatic hyperplasia in a subject which comprises
10 administering to the subject a therapeutically effective amount of any one of the compounds disclosed herein.

The invention provides a method of lowering intraocular pressure in a subject which comprises administering to
15 the subject a therapeutically effective amount of any one of the compounds disclosed herein.

The invention further provides a method of inhibiting cholesterol synthesis in a subject which comprises
20 administering to the subject a therapeutically effective amount of any one of the compounds disclosed herein.

The invention has general utility in providing a method of treating diseases mediated by α_1 receptors in a subject
25 which comprises administering to the subject a therapeutically effective amount of any one of the compounds disclosed herein.

Throughout this application the term "compound" is used
30 to refer both to unresolved racemic mixtures and to each of the optically resolved enantiomers in those cases where a given compound is optically active.

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The invention additionally provides a method of treating diseases mediated by α_1 receptors in a subject which comprises administering to the subject a therapeutically effective amount of any one of the compounds of the preferred embodiments.

Certain preferred embodiments of this invention are denoted in the Experimental Details provided herein as 2, 29, 38, 41, 42, 45, 47, 56, 61, 73, 81, 82, 83, 93, 166, 171, 178, 180, 181, 182, 185, 192, 193, 197, 198, 199, 201, 202, 207 and 233.

The dihydropyridine derivatives disclosed herein are potent, selective α_1 antagonists with weak calcium channel antagonist activity, and, it is anticipated, will be useful in providing a novel treatment for benign prostatic hyperplasia. This therapeutic use is supported by data presented in Tables 2 and 3 hereinbelow, which illustrate the beneficial effects of representative examples of these compounds in well established models of prostate contraction. In addition, the compounds disclosed herein may also be useful as cardiovascular antihypertensive agents, as inhibitors of cholesterol synthesis, and as agents for decreasing intraocular pressure in a mammalian eye, as well as for treating male erectile dysfunction, congestive heart failure, Raynaud's disease, and multidrug resistance.

The present invention therefore provides a method of treating benign prostatic hyperplasia, a method of reducing cardiovascular hypertension, cholesterol synthesis, and intraocular pressure in a mammalian eye, a method for treating male erectile dysfunction, congestive heart failure, Raynaud's disease, and multidrug resistance. For example, the method of treating benign prostatic hyperplasia comprises administering a quantity of any of the claimed dihydro-

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pyridines effective to treat benign prostatic hyperplasia. The drug may be administered to a patient afflicted with benign prostatic hyperplasia by any conventional route of administration, including, but not
5 limited to, intravenous, intramuscular, oral, subcutaneous, intratumoral, intradermal, and parenteral. The effective quantity is between 0.001 mg and 10.0 mg per kg of subject body weight.

10 The present invention also provides compounds useful for preparing a pharmaceutical composition comprising any of the claimed dihydropyridines disclosed herein and a pharmaceutically acceptable carrier. The composition may contain between 0.1 mg and 500 mg of the claimed
15 compound, and may be constituted in any form suitable for the mode of administration selected. Compositions suitable for oral administration include solid forms, such as pills, capsules, granules, tablets, and powders, and liquid forms, such as solutions, syrups, elixers, and
20 suspensions. Forms useful for parenteral administration include sterile solutions, emulsions, and suspensions.

The drug may otherwise be prepared as a sterile solid composition which may be dissolved or suspended at the
25 time of administration using sterile water, saline, or other appropriate sterile injectible medium. Carriers are intended to include necessary and inert binders, suspending agents, lubricants, flavorants, sweeteners, preservatives, dyes, and coatings.

30 Optimal dosages to be administered may be determined by those skilled in the art, and will vary with the particular dihydropyridine in use, the strength of the preparation, the mode of administration, and the
35 advancement of the disease condition. Additional factors depending on the particular patient being treated will result in a need to adjust dosages, including patient age, weight, gender, diet, and time of administration.

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The following Experimental Details are set forth to aid in an understanding of the invention, and are not intended, and should not be construed, to limit in any way the invention set forth in the claims which follow
5 thereafter.

Experimental Details.

General Methods

10 Four general synthetic methods were used to synthesize the compounds of the invention. These methods are illustrated in Reaction Schemes 1-4. The symbols R, A, B, and C, and the variable n are defined by the Examples.

15 Method A:

Example 1 is illustrative of Method A, which is outlined in Reaction Scheme 1.

20

EXAMPLE 1

4,4-Diphenylpiperidine hydrochloride. A mixture of 4-piperidone monohydrate hydrochloride (15.0 g, 97.6 mmol, 1.00 equiv) and AlCl₃ (130 g, 976 mmol, 10.0 equiv) in
25 anhydrous benzene (600 mL) was stirred at reflux for 4 hours. The mixture was cooled to room temperature, poured into ice (300 g) and water (50 mL), and filtered. The solid was washed with toluene and dried to afford 19.2 g (72%) of off-white solid, which was characterized
30 spectroscopically.

3-(4,4-Diphenylpiperidin-1-yl)propionitrile. To a suspension of 4,4-diphenylpiperidine hydrochloride (195 mg, 0.712 mmol, 1.0 equiv) in EtOH (1.5 mL) was added Et₃N
35 (0.25 mL, 1.8 mmol, 2.6 equiv) followed by acrylonitrile (0.13 mL, 2.01 mmol, 2.8 equiv). The resulting solution was stirred at room temperature under argon for 15

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minutes and then concentrated. Water was added, and the mixture was extracted three times with EtOAc. The combined organic extracts were dried over MgSO_4 and concentrated to give 170 mg (87%) of tan solid, which was
5 characterized spectroscopically and used for the next reaction without purification.

1-(3-Aminopropyl)-4,4-diphenylpiperidine. To a stirred solution of 3-(4,4-diphenylpiperidin-1-yl)propionitrile (2.00 g, 6.89 mmol, 1.0 equiv) in anhydrous THF (20 mL) under argon was added a solution of BH_3 in THF (1.0 M, 24.1 mL, 24 mmol, 3.5 equiv) at room temperature. The mixture was refluxed for 4.5 hours and then cooled to room temperature. Aqueous HCl (6 N, 50 mL) was added and
15 stirring was continued for 1 hour. The mixture was basified to pH 9 by addition of 6 N aq. NaOH, extracted 3 times with CH_2Cl_2 , dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , EtOAc-MeOH-isopropylamine 9:1:0 to 4:1:0.2) to give 1.35
20 g (66%) of tan solid, which was characterized spectroscopically.

N-(3-(4,4-Diphenylpiperidin-1-yl)propyl)acetoacetamide. Diketene (0.44 mL, 5.7 mmol, 1.3 equiv, Aldrich) was
25 added at room temperature to a stirred solution of 1-(3-aminopropyl)-4,4-diphenylpiperidine (1.288 g, 4.37 mmol, 1.0 equiv) in anhydrous toluene (15 mL) under argon, and stirring was continued for 48 hours. The mixture was concentrated to give 1.294 g (78%) of white solid, which
30 was used for the next reaction without purification. An analytically pure sample was obtained by flash chromatography (SiO_2 , EtOAc-MeOH- Et_3N 9:1:0 to 6:1:0.1) and characterized spectroscopically.

35 4-(4-Trifluoromethylphenyl)-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (1). N-(3-(4,4-diphenylpiperid-

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in-1-yl)propyl)acetoacetamide (229 mg, 0.61 mmol) was mixed with methyl 3-aminocrotonate (70 mg, 0.61 mmol) and p-trifluoromethylbenzaldehyde (83 μ l, d 1.275, 0.61 mmol) in 2-propanol (5 mL). The mixture was heated at reflux for 3 days. The precipitate which formed upon cooling to room temperature was filtered off to give a pale yellow solid (160 mg). Recrystallization from 2-propanol afforded white crystals (117 mg, 31% yield): mp 228-231°C. Anal. Calcd. for $C_{37}H_{40}F_3N_3O_3$: C, 70.35; H, 6.38; N, 6.65. Found: C, 70.26; H, 6.40; N, 6.51.

Method B:

Example 2 is illustrative of Method B, which is outlined in Reaction Scheme 2.

EXAMPLE 2

5-Carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamido}pyridine (2). A solution of 3-aminocrotonamide (6.028 g, 60.21 mmol), 4-nitrobenzaldehyde (6.066 g, 40.14 mmol) and 2-cyanoethyl acetoacetate (6.227 g, 40.14 mmol) in 125 mL of EtOH was refluxed for 48 hrs. The reaction mixture was filtered and the filtrate was concentrated to give a brown oil. This brown oil was dissolved in 250 mL of $CHCl_3$ (with addition of a small amount of acetone to give a homogeneous solution), washed with water (2 x 100 mL) and dried over Na_2SO_4 . After filtration and removal of solvent, the residue was dissolved into 200 mL of MeOH and treated with 100 mL 2N KOH solution at 0°C for 30 min. The MeOH was removed in vacuo and the aqueous layer was diluted with 100 mL of water and washed with AcOEt (2x100 mL). With stirring, the aqueous layer was acidified to pH=1 by addition of 6 N hydrochloric acid. The yellow precipitate was collected by filtration, washed with 10 mL of cold water

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and dried in vacuo to afford 5.877 g (46.1% yield for two steps) of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid as a yellow powder.

5

A suspension of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (150 mg, 0.473 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (90.6 mg, 0.473 mmol) in 15 mL of CH_2Cl_2 was stirred at 0°C for 20 min. To this suspension was added a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (139 mg, 0.473 mmol) in 2 mL of CH_2Cl_2 . The mixture was stirred at refluxing conditions overnight. The formation of a clear solution indicated completion of the reaction. The mixture was washed with water (2 × 10 mL) followed by brine (10 mL). After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was precipitated from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to afford a yellowish powder (165 mg, 58.8 %): m.p. 212-215 °C. Calcd. for $\text{C}_{35}\text{H}_{39}\text{N}_5\text{O}_4$: C 70.79, H 6.63, N 11.79; Found: C 71.00, H 6.79, N 11.51.

(+) and (-)-2. The enantiomers of 2 were separated on a chiral HPLC column as follows. Four injections of the racemate (16 mg per injection in 2 ml of EtOH) were made onto a Chiralpak AS column (20 × 250 mm, Daicel), which was eluted with EtOH-hexane-diethylamine (10:90:0.05) at a flowrate of 9.0 ml/min with UV detection at 300 nm. The retention times for the two enantiomers were 50 ((+)-isomer) and 65 ((-)-isomer) min respectively. The desired compounds were collected and precipitated from $\text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2$ to give yellowish powders.

(+)-isomer: $[\alpha]_D^{20} = +91.2^\circ$ (c 0.32, CHCl_3). Calcd. for $\text{C}_{35}\text{H}_{39}\text{N}_5\text{O}_4$: C 70.79, H 6.63, N 11.79; Found: C 70.53, H 6.41, N 11.50.

(-)-isomer: $[\alpha]_D^{20} = -90.0^\circ$ (c 0.38, CHCl_3). Calcd. for

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$C_{35}H_{39}N_5O_4$: C 70.79, H 6.63, N 11.79; Found: C 70.58, H 6.39, N 11.57.

Method C:

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Example 3 is illustrative of Method C, which is outlined in Reaction Scheme 3.

EXAMPLE 3

10

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(4-nitro-phenyl)-5-{N-[4-(4-phenylpiperidin-1-yl)butyl]}carboxam-
idopyridine hydrochloride hydrate (3). A solution of
9.61 g of benzyl acetoacetate (50.0 mmol), 5.87 g of
15 methyl 3-aminocrotonate (51.0 mmol), and 7.71 g of 4-
nitrobenzaldehyde (51.0 mmol) in 200 mL of isopropanol
was heated at reflux temperature for 2 days. The
reaction mixture was cooled and concentrated. The crude
product was charged with 250 mL of methanol and 1.10 g of
20 10% Pd/C, and the mixture was hydrogenated using the
balloon method for 24 h. The reaction mixture was
filtered through celite 545, concentrated in vacuo,
partitioned between water (200 mL, containing 3.0 g of
NaOH) and ethyl acetate (100 mL). The aqueous phase was
25 washed further with 2 X 50 mL of ethyl acetate, and
acidified with concentrated HCl (pH = 2). The separated
oil was extracted with 2 X 200 mL of ethyl acetate, and
2 X 200 mL of dichloromethane. The combined organic
extracts were dried ($MgSO_4$), and the solvent was removed
30 in vacuo to give 3.52 g of 1,4-dihydro-3-methoxycarbonyl-
2,6-dimethyl-4-(4-nitrophenyl)-5-carboxylic acid (21%) as
a yellow solid: mp 172-175 °C (decomp.); Anal. Calcd for
 $C_{16}H_{16}N_2O_6$: C, 57.83; H, 4.85; N, 8.43. Found: C, 58.05; H,
4.79; N, 8.26.

35

4-Hydroxypiperidine (10.0 g, 98.9 mmol, 1.00 equiv) and
 $AlCl_3$ (105.5 g, 791.2 mmol, 8.0 equiv) were stirred in

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refluxing benzene (350 mL) under a CaSO_4 drying tube for 85 hours. The mixture was cooled to room temperature and poured carefully into ice (500 g) and water (50 mL) with stirring. With ice water cooling, the pH was adjusted to 5 10-11 by addition of solid NaOH. The resulting mixture was extracted with EtOAc (3 x 250 mL). The combined organic solutions were washed with brine, dried over MgSO_4 , and concentrated to give 6.5 g of 4-phenylpiperidine (yellow solid, 40%), which was 10 characterized spectroscopically.

A suspension of 4-phenylpiperidine (5.20 g, 32.2 mmol, 1.00 equiv), 4-bromobutyronitrile (4.81 mL, 48.4 mmol, 1.50 equiv), potassium carbonate (11.14 g, 80.6 mmol, 15 2.50 equiv), and potassium iodide (266 mg, 12.9 mmol, 0.4 equiv) in n-butanol (60 mL) and 1,4-dioxane (60 mL) was stirred at reflux under argon for 48 hours. The mixture was cooled to room temperature and concentrated. The residue was purified by flash chromatography (SiO_2 , MeOH-EtOAc 1:19) to afford 3.95 g of 4-(4-phenylpiperidin-1-yl)butyronitrile (white solid, 53%), which was character- 20 ized spectroscopically.

To a stirred solution of 4-(4-phenylpiperidin-1-yl)butyronitrile (3.81 g, 16.7 mmol, 1.0 equiv) in 25 anhydrous THF (20 mL) under argon was added a solution of BH_3 in THF (1.0 M, 58.5 mL, 58 mmol, 3.5 equiv) at room temperature. The mixture was refluxed for 4.5 hours and then cooled to room temperature. Aqueous HCl (6 N, 100 30 mL) was added and stirring was continued for 2 hours at 55-60 °C. The mixture was basified to pH 9 by addition of 6 N aq. NaOH and extracted with CH_2Cl_2 (3 x 100 mL). The combined organic solutions were dried over MgSO_4 and concentrated. The residue was dissolved in CH_2Cl_2 (20 mL) 35 and treated with HCl in ether (1.0 M, 35 mL). The solvents were removed, ether (200 mL) was added, the mixture was filtered, and the filter cake was washed with

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ether. Water (50 mL) was added to the resulting white solid, the pH was adjusted to 10-11 with 1 M NaOH, and the aqueous phase was extracted with CH_2Cl_2 (3 x 100 mL). Drying over MgSO_4 followed by removal of solvents gave
5 3.54 g of 1-(4-aminobutyl)-4-phenylpiperidine (light yellow solid, 91%) which was characterized spectroscopically.

Anhydrous CH_2Cl_2 (15 mL) was added to a mixture of 1,4-
10 dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophenyl)-5-carboxylic acid (596 mg, 1.79 mmol, 1.00 equiv), 1,3-dicyclohexylcarbodiimide (554 mg, 2.68 mmol, 1.50 equiv), and 4-(*N,N*-dimethylamino)pyridine (241 mg, 1.97 mmol, 1.10 equiv) and the resulting solution was stirred for 1
15 hour at room temperature. A solution of 1-(4-aminobutyl)-4-phenylpiperidine (500 mg, 2.15 mmol, 1.20 equiv) in CH_2Cl_2 (3 mL) was injected and the mixture was stirred at reflux for 3 hours. The resulting suspension was cooled to room temperature, diluted with EtOAc (100
20 mL) and filtered. The solid was washed with EtOAc (3 x 5 mL). The combined filtrates were washed with saturated aqueous ammonium chloride (3 x 50 mL) and brine (50 mL), dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 - NH_3 in MeOH
25 (0.67 M), 90:10) to afford 595 mg (61%) of yellow solid, which was characterized spectroscopically. To a solution of this product in CH_2Cl_2 (10 mL) was added HCl in ether (1.0 M, 1.5 mL, 1.4 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and
30 added dropwise to ether (30 mL) with swirling to give, after filtration, 430 mg of 3 hydrochloride hydrate (yellow solid): m.p. 136-137 °C; Anal. Calcd. for $\text{C}_{21}\text{H}_{25}\text{N}_4\text{O}_3 \cdot \text{HCl} \cdot 0.75 \text{H}_2\text{O}$: C, 62.41; H, 6.84; N, 9.39. Found: C, 62.46; H, 6.76; N, 9.33.

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Method D:

Example 4 is illustrative of Method D, which is outlined

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in Reaction Scheme 4.

EXAMPLE 4

5 **2-Cyanoethyl 3-Oxopentanoate.** A mixture of 4.86 g of ethyl propionylacetate (33.7 mmol) and 2.00 g of 3-hydroxypropionitrile (28.1 mmol) were placed in a round bottom flask (magnetically stirred) equipped with a short distillation path. The resulting mixture was gradually
10 heated to 180-205°C in an oil bath. The distillate was collected (1.2 mL). The mixture was then cooled to room temperature and the residue was distilled under reduced pressure to give 2.64 g of product: bp 95-98°C (0.5 mm Hg). The product was used in the next step after
15 spectral characterization.

5-Benzylloxycarbonyl-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine, Hydrochloride Salt, Hydrate (4). A stirred solution of 19.2 g of benzyl 3-aminocrotonate (100 mmol, Davoll, J. J. Chem. Soc. 1953, 3802), 16.9 g of 2-cyanoethyl 3-oxopentanoate (100 mmol), and 15.1 g of 4-nitrobenzaldehyde (100 mmol) in 100 mL of
25 ethanol were heated at reflux temperature for 4 h, cooled, filtered and the solids were washed with 4 X 50 mL of acetone. To the filtrate was added 5.20 g of NaOH in 200 mL of water, and the resulting mixture was stirred at room temperature for 12 hrs. The reaction mixture was
30 partitioned between 200 mL of additional water and 0.5 L of dichloromethane, separated, washed with 3 X 0.5 L of dichloromethane, acidified with concentrated HCl (pH = 2), the precipitated solids were filtered, and the solids were washed with 5 X 50 mL of EtOAc. More solids
35 appeared in the filtrate. The solids were filtered, and the filtrate was concentrated in vacuo. The residue was triturated with acetone, cooled to -78 °C, the

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precipitated solids were filtered, and washed with 2 X 50 mL of cold acetone (-78 °C) to give 5.20 g of 3-benzyloxycarbonyl-2-ethyl-6-methyl-4-(4-nitro)phenylpyridine-5-carboxylic acid as a yellow powder (12%): mp 209-210 °C; Anal. Calcd for $C_{22}H_{22}N_2O_6 \cdot 0.5H_2O$: C, 64.03; H, 5.37; N, 6.49. Found: C, 64.39; H, 4.83; N, 6.41.

A mixture of 3.12 g of 3-benzyloxycarbonyl-2-ethyl-6-methyl-4-(4-nitro)phenylpyridine-5-carboxylic acid (6.55 mmol), 2.03 g of DCC (9.83 mmol), and 880 mg of DMAP (7.21 mmol) in 20 mL of dry dichloromethane was stirred at room temperature for 1h. 1-(3-aminopropyl)-4,4-diphenylpiperidine (2.06 g, 7.86 mmol) was added the mixture was heated at reflux temperature for 2 hrs. The reaction mixture was cooled, filtered, and chromatographed on 400 g of silica packed with 5% MeOH-EtOAc. The column was eluted with 5% (1 L), 10% (1 L), 15% (1 L), and 20% (2 L) MeOH-EtOAc to give 3.84 g of 5-benzyloxycarbonyl-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamidopyridine (95%) as a yellow foamy solid. Hydrochloride Salt: The free base (72 mg) was dissolved in 2 mL of dichloromethane and added to 7 mL of 0.25 M HCl in ether. The precipitate was collected, washed with 5 mL of ether, and dried to give a yellow powder: mp 195-198 °C (decomp.). Anal. Calcd for $C_{33}H_{36}N_4O_5 \cdot HCl$: C, 68.56; H, 6.56; N, 7.44. Found: C, 68.38; H, 6.20; N, 7.40.

30

EXAMPLE 5

1,4-Dihydro-5-benzyloxycarbonyl-2,6-dimethyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)-4-(4-pyridyl)pyridine (5). This compound was prepared according to Method A. N-(3-(4,4-diphenylpiperidin-1-yl)propyl)acetoacetamide (200 mg, 0.53 mmol) was mixed with methyl 3-aminocrotonate (61 mg, 0.53 mmol) and 4-pyridine-

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carboxaldehyde (51 ul, d 1.122, 0.53 mmol) in 2-propanol (5 mL). The mixture was heated at reflux for 2 days. The precipitate which formed upon cooling to room temperature was filtered off to give an almost white solid (95 mg). Recrystallization from 2-propanol afforded white crystals (63 mg, 21% yield): mp 224-226°C (dec.). Anal. Calcd. for $C_{35}H_{40}N_4O_3$: C, 74.44; H, 7.14; N, 9.92. Found: C, 74.43; H, 7.23; N, 9.83.

10

EXAMPLE 6

4-Cyclohexyl-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (6). This compound was prepared according to Method A. N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.53 mmol) was mixed with methyl 3-aminocrotonate (61 mg, 0.53 mmol) and cyclohexanecarboxaldehyde (64 ul, d 0.926, 0.53 mmol) in 2-propanol (5 mL). The mixture was heated at reflux for 2 days and then concentrated to a pale yellow foam. It was dissolved in chloroform and flash chromatographed over silica gel (14 g) eluting with EtOAc/Hexane/ Et_3N (40:20:3 and then 16:4:1) to give a pale yellow foam (114 mg). It was recrystallized from acetone/hexane to afford white crystals (63 mg, 21% yield): mp 171-174°C. Anal. Calcd. for $C_{36}H_{47}N_3O_3$: C, 75.89; H, 8.31; N, 7.37. Found: C, 75.86; H, 8.09; N, 7.00.

30

EXAMPLE 7

4-(4-Biphenyl)-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (7). This compound was prepared according to Method A. N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.53 mmol) was mixed with methyl 3-aminocrotonate (61 mg, 0.53 mmol) and 4-biphenylcarboxaldehyde (96 mg, 0.53 mmol) in 2-propanol

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(5 mL). The mixture was heated at reflux for 3 days before it was concentrated to a yellow foam. It was dissolved in chloroform and flash chromatographed over silica gel (15 g) eluting with EtOAc/Hexane/Et₃N (50:10:3) to give a yellow oil which partially solidified (128 mg). It was recrystallized from EtOAc/Hexane to afford white crystals (55 mg, 16% yield): mp 136-139°C. Anal. Calcd. for C₄₂H₄₅N₃O₃: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.54; H, 6.92; N, 6.37.

10

EXAMPLE 8

4-Benzyl-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (8). This compound was prepared according to Method A. N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (180 mg, 0.48 mmol) was mixed with methyl 3-aminocrotonate (55 mg, 0.48 mmol) and phenylacetaldehyde (62 μ l, d 1.027, 90%, 0.48 mmol) in 2-propanol (5 mL). The mixture was heated at reflux for 1 day before it was concentrated to a yellow foam. It was dissolved in chloroform and flash chromatographed over silica gel (15 g) eluting with EtOAc/Hexane/Et₃N (15:5:2) to give a pale yellow foam (132 mg). It was recrystallized from EtOAc/Hexane to afford a white solid (81 mg, 29% yield): mp 175-177°C. Anal. Calcd. for C₃₇H₄₃N₃O₃: C, 76.92; H, 7.50; N, 7.27. Found: C, 76.81; H, 7.68; N, 7.07.

30

EXAMPLE 9

1,4-Dihydro-3-methoxycarbonyl-2,6-Dimethyl-4-(1-oxido-4-pyridyl)-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (9). This compound was prepared according to Method A. N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (205 mg, 0.54 mmol) was mixed with methyl 3-aminocrotonate (62 mg, 0.54 mmol) and 4-

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pyridinecarboxaldehyde N-oxide (67 mg, 0.54 mmol) in 2-propanol (5 mL). The mixture was heated at reflux for 2 days before it was concentrated to a dark green foam. It was dissolved in chloroform and flash chromatographed
5 over silica gel (15 g) eluting with EtOAc/MeOH/Et₃N (10:2:1) to give a yellow foam (171 mg). Trituration with EtOAc afforded a pale yellow powder (96 mg, 31% yield): mp 206-209°C (dec.). Anal. Calcd. for C₃₅H₄₀N₄O₄·1/4 H₂O: C, 71.83; H, 6.98; N, 9.57. Found: C, 71.61; H, 6.72; N,
10 9.36.

EXAMPLE 10

4-(4-Chlorophenyl)-1,4-dihydro-5-methoxycarbonyl-2,6-
15 Dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (10). This compound was prepared according to Method A. N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.53 mmol) was mixed with methyl 3-aminocrotonate (61 mg, 0.53 mmol) and 4-
20 chlorobenzaldehyde (74 mg, 0.53 mmol) in 2-propanol (5 mL). The mixture was heated at reflux for 3 days and the precipitate, after cooling to room temperature, was filtered off to give an almost white solid (134 mg). It was recrystallized twice from chloroform/hexane to afford
25 white crystals (99 mg, 31% yield): mp 240-242°C. Anal. Calcd. for C₃₆H₄₀ClN₃O₃·1/2 H₂O: C, 71.21; H, 6.81; N, 6.92. Found: C, 70.83; H, 6.50; N, 6.73.

EXAMPLE 11

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1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(3,4-methylenedioxyphenyl)-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (11). This compound was prepared according to Method A. A mixture of N-(3-(4,4-
35 diphenylpiperidin-1-yl)propyl) acetoacetamide (322 mg, 0.85 mmol), methyl 3-aminocrotonate (98 mg, 0.85 mmol) and piperonal (128 mg, 0.85 mmol) was heated at reflux in

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2-propanol (7 mL) for 1 day and then in 1-butanol (7 mL) for another day. Evaporation of the solvent gave an orange foam which was dissolved in chloroform and flash chromatographed over silica gel (20 g) eluting with
5 EtOAc/Hexane/Et₃N (50:10:3) to afford a yellow foam (144 mg). Recrystallization from EtOAc/Hexane gave yellow crystals (64 mg, 12% yield): mp 197-200°C. Anal. Calcd. for C₃₇H₄₁N₃O₅: C, 73.12; H, 6.80; N, 6.91. Found: C, 73.12; H, 6.71; N, 6.69.

10

EXAMPLE 12

4-(4-Cyanophenyl)-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (12). This compound was prepared
15 according to Method A. N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.53 mmol) was mixed with methyl 3-aminocrotonate (61 mg, 0.53 mmol) and 4-cyanobenzaldehyde (69 mg, 0.53 mmol) in 2-propanol (5
20 mL). The mixture was heated at reflux for 3 days and then concentrated to a yellow oil. It was flash chromatographed over silica gel (18 g) eluting with EtOAc/Et₃N (10:1) to give a yellow foam (187 mg). It was recrystallized from MeOH/ether at -20°C to afford pale
25 yellow crystals (146 mg, 47% yield): mp 115-118°C. Anal. Calcd. for C₃₇H₄₀N₄O₃: C, 75.48; H, 6.85; N, 9.52. Found: C, 75.27; H, 6.82; N, 9.39.

EXAMPLE 13

30

1,4-Dihydro-4-(4-iodophenyl)-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (13). This compound was prepared according to Method A. N-(3-(4,4-
35 diphenylpiperidin-1-yl)propyl) acetoacetamide (186 mg, 0.49 mmol) was mixed with methyl 3-aminocrotonate (57 mg, 0.50 mmol) and 4-iodobenzaldehyde (114 mg, 0.49 mmol) in

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2-propanol (5 mL) and heated at reflux for 2 days. The solution was cooled to room temperature and then refrigerated to give a pale yellow solid. It was recrystallized from 2-propanol/hexane to afford white
5 crystals (44 mg, 13% yield): mp 228-230°C (dec.). Anal. Calcd. for $C_{36}H_{40}IN_3O_3$: C, 62.70; H, 5.85; N, 6.09. Found: C, 62.47; H, 5.82; N, 5.92.

EXAMPLE 14

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1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)-4-(3-pyrid-
yl)pyridine (14). This compound was prepared according to Method A. N-(3-(4,4-Diphenylpiperidin-1-yl)propyl)
15 acetoacetamide (200 mg, 0.53 mmol) was mixed with methyl 3-aminocrotonate (61 mg, 0.53 mmol) and 3-pyridine-carboxaldehyde (50 μ l, d 1.135, 0.53 mmol) in 2-propanol (5 mL). The mixture was heated at reflux for 3 days. The resulting precipitate was cooled to room temperature
20 and then filtered off to give an almost white solid (115 mg). Recrystallization from MeOH at -20°C afforded white crystals (56 mg, 19% yield): mp 244-247°C (dec.). Anal. Calcd. for $C_{35}H_{40}N_4O_3$: C, 74.44; H, 7.14; N, 9.92. Found: C, 74.24; H, 7.16; N, 9.73.

25

EXAMPLE 15

4-(4-Bromophenyl)-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-
yl)propyl)carboxamido)pyridine (15). This compound was
30 prepared according to Method A. N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (181 mg, 0.48 mmol) was mixed with methyl 3-aminocrotonate (55 mg, 0.48 mmol) and 4-bromobenzaldehyde (88 mg, 0.48 mmol) in
35 2-propanol (5 mL) and heated at reflux for 2 days. The precipitate was filtered off and washed with 2-propanol to give an almost white solid (61 mg). It was

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recrystallized from ethanol at -20°C to afford white crystals (38 mg, 12% yield): mp $244-247^{\circ}\text{C}$ (dec.). Anal. Calcd. for $\text{C}_{36}\text{H}_{40}\text{BrN}_3\text{O}_3$: C, 67.28; H, 6.27; N, 6.54. Found: C, 67.02; H, 6.43; N, 6.33.

5

EXAMPLE 16

4-(4-Chloro-3-nitrophenyl)-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (16). This compound was prepared according to Method A. N-(3-(4,4-Diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.53 mmol) was mixed with methyl 3-aminocrotonate (61 mg, 0.53 mmol) and 4-chloro-3-nitrobenzaldehyde (98 mg, 0.53 mmol) in 2-propanol (5 mL) and heated at reflux for 2 days. Then the solvent was evaporated to give a brown foam. It was dissolved in CHCl_3 and flash chromatographed over silica gel (17 g) eluting with EtOAc/ Et_3N (10:1) to yield a yellow foam (182 mg). Trituration with EtOAc afforded a pale yellow solid (107 mg, 31% yield): mp $178-181^{\circ}\text{C}$. Anal. Calcd. for $\text{C}_{36}\text{H}_{39}\text{ClN}_4\text{O}_5$: C, 67.23; H, 6.11; N, 8.71. Found: C, 67.04; H, 6.33; N, 8.61.

EXAMPLE 17

25

3-(4-Phenylpiperidin-1-yl)propionitrile. Acrylonitrile (3.1 mL, 44 mmol, 2.5 equiv) was added to a solution of 4-phenylpiperidine (3.0 g, 18 mmol, 1.0 equiv) in EtOH (40 mL) and the mixture was stirred at room temperature for 1.5 hours. The volatiles were removed to give 3.8 g of pure product (brown oil, 99%), which was characterized spectroscopically.

1-(3-Aminopropyl)-4-phenylpiperidine. To a stirred solution of 3-(4-phenylpiperidin-1-yl)propionitrile (5.1 g, 24 mmol, 1.0 equiv) in anhydrous THF (20 mL) under argon was added a solution of BH_3 in THF (1.0 M, 83 mL, 83

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mmol, 3.5 equiv) at room temperature. The mixture was refluxed for 4.5 hours and then cooled to room temperature. Aqueous HCl (6 N, 130 mL) was added and stirring was continued for 2 hours at 50-70 °C. The mixture was basified to pH 9 by addition of 6 N aq. NaOH and extracted with EtOAc (100 mL) and CH₂Cl₂ (3 x 100 mL). The combined organic solutions were dried over MgSO₄ and concentrated. The residue was dissolved in CH₂Cl₂ (20 mL) and treated with HCl in ether (1.0 M, 50 mL). The solvents were removed, ether (250 mL) was added, the mixture was filtered, and the filter cake was washed with ether. Water (60 mL) was added to the resulting white solid, the pH was adjusted to 10-11 with 1 M NaOH, and the aqueous phase was extracted three times with CH₂Cl₂. Drying over MgSO₄ followed by removal of solvents gave 4.5 g (87%) of pure product (light brown solid), which was characterized spectroscopically.

N-(3-(4-Phenylpiperidin-1-yl)propyl)acetoacetamide.

Diketene (1.64 mL, 21.3 mmol, 1.50 equiv) was added at 0 °C to a stirred solution of 1-(3-aminopropyl)-4-phenylpiperidine (3.10 g, 14.2 mmol, 1.00 equiv) in anhydrous THF (30 mL) under argon, and stirring was continued at room temperature for 1 hour. The mixture was concentrated to give 4.50 g (100%) of viscous orange oil, which was characterized spectroscopically and used for the next reaction without purification.

4-(4-Chloro-3-nitrophenyl)-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4-phenylpiperidin-1-yl)propyl)carboxamido)pyridine (17). This compound was prepared according to Method A. N-(3-(4-phenylpiperidin-1-yl)propyl) acetoacetamide (221 mg, 0.73 mmol) was mixed with methyl 3-aminocrotonate (84 mg, 0.73 mmol) and 4-chloro-3-nitrobenzaldehyde (136 mg, 0.73 mmol) in 2-propanol (7 mL) and heated at reflux for 2 days. Then the solvent was evaporated to give a yellow foam. It was

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dissolved in CHCl_3 and flash chromatographed over silica gel (19 g) eluting with $\text{EtOAc}/\text{Et}_3\text{N}$ (20:1) to yield a yellow foam (194 mg). Recrystallization from EtOAc afforded yellow crystals (119 mg, 29% yield): mp 191-
5 192°C. Anal. Calcd. for $\text{C}_{30}\text{H}_{35}\text{ClN}_4\text{O}_5$: C, 63.54; H, 6.22; N, 9.88. Found: C, 63.65; H, 6.26; N, 9.64.

EXAMPLE 18

10 1,4-Dihydro-4-(4-isopropylphenyl)-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (18). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg,
15 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528 mmol), and 4-isopropylbenzaldehyde (80.1 μL , 0.528 mmol) in 2-propanol (5 mL) was refluxed for 48 hrs. Then the solvent was removed, and the residue was chromatographed (Flash silica; hexane : EtOAc : Et_3N = 50 : 50 : 3,
20 hexane : EtOAc : Et_3N = 10 : 90 : 6, EtOAc : Et_3N = 10 : 1) to give a yellow solid. It was recrystallized from EtOAc and hexane to afford white crystals (140 mg, 44%): m. p. 163.0-163.5 °C. Anal. Calcd. for $\text{C}_{39}\text{H}_{47}\text{N}_3\text{O}_3$: C, 77.32, H, 7.82, N, 6.94. Found: C, 77.29, H, 7.80, N,
25 6.84.

EXAMPLE 19

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(4-methylphenyl)-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (19). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528
35 mmol), and 4-methylbenzaldehyde (62.3 μL , 0.528 mmol) in 2-propanol (5 mL) was refluxed for 72 hrs. Then the solvent was removed, and the residue was chromatographed

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(Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow solid. It was recrystallized from EtOAc and hexane to afford white crystals (100 mg, 33%):
5 m. p. 234.0-235.0 °C. Anal. Calcd. for C₃₇H₄₃N₃O₃·1/2H₂O: C, 75.73, H, 7.56, N, 7.16. Found: C, 75.91, H, 7.33, N, 6.94.

EXAMPLE 20

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4-(4-Fluorophenyl)-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (20). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg,
15 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528 mmol), and 4-fluorobenzaldehyde (56.6 ul, 0.528 mmol) in 2-propanol(5 mL) was refluxed for 72 hrs. Then the solvent was removed, and the residue was chromatographed
20 (Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give white crystals (100 mg, 33%): m. p. 251.0-251.5 °C. Anal. Calcd. for C₃₆H₄₀N₃O₃F: C, 74.33, H, 6.93, N, 7.22, F, 3.27. Found: C, 74.08, H, 7.13, N, 6.71, F,
25 3.38.

EXAMPLE 21

1,4-Dihydro-3-methoxycarbonyl-4-(4-methoxyphenyl)-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (21). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528
35 mmol), and 4-methoxybenzaldehyde (64.2 ul, 0.528 mmol) in 2-propanol(5 mL) was refluxed for 96 hrs. Then the solvent was removed, and the residue was chromatographed

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(Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow oil. It was recrystallized from EtOAc and hexane to afford white crystals (100 mg, 31%):
5 m. p. 212.0-213.0 °C. Anal. Calcd. for C₃₇H₄₃N₃O₄: C, 74.84, H, 7.30, N, 7.08. Found: C, 74.61, H, 7.26, N, 6.85.

EXAMPLE 22

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1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(2-naphthyl)-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (22). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg,
15 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528 mmol), and 2-naphthaldehyde (84.0 mg, 0.528 mmol) in 2-propanol(5 mL) was refluxed for 72 hrs. Then the solvent was removed, and the residue was chromatographed (Flash
20 silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow solid. It was recrystallized from EtOAc and hexane to afford white crystals (100 mg, 31%): sublimes at R.T. Anal. Calcd. for C₄₀H₄₃N₃O₃: C, 78.27, H, 7.06, N,
25 6.85. Found: C, 78.31, H, 7.28, N, 6.64.

EXAMPLE 23

4-(3-Furyl)-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (23). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528 mmol), and 3-furaldehyde
35 (46.7 ul, 0.528 mmol) in 2-propanol(5 mL) was refluxed for 72 hrs. Then the solvent was removed, and the residue was chromatographed (Flash silica; hexane :

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EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow oil. It was recrystallized from EtOAc and hexane to afford white crystals (40 mg, 14%): m. p. 225.0-226.0 °C. Anal. Calcd. for C₃₄H₃₉N₃O₄: C, 73.75, H, 7.10, N, 7.59. Found: C, 73.48, H, 6.92, N, 7.30.

EXAMPLE 24

10 4-(3,4-Dichlorophenyl)-1,4-dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(3-(4,4-diphenylpiperidin-1-yl)propylcarboxamido)pyridine (24). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg,
15 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528 mmol), and 3,4-dichlorobenzaldehyde (92.4 mg, 0.528 mmol) in 2-propanol(5 mL) was refluxed for 72 hrs. Then the solvent was removed, and the residue was chromatographed (Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3,
20 hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow oil. It was recrystallized from EtOAc and hexane to afford white crystals (75 mg, 23%): m. p. 177.0-178.0 °C. Anal. Calcd. for C₃₆H₃₉N₃O₃Cl₂: C, 68.35, H, 6.21, N, 6.64, Cl, 11.20. Found: C, 68.27, H,
25 5.91, N, 6.45, Cl, 10.93.

EXAMPLE 25

1,4-Dihydro-3-methoxycarbonyl-4-(4-methoxycarbonylphenyl)-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (25). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528
35 mmol), and methyl 4-formylbenzoate (86.7 mg, 0.528 mmol) in 2-propanol(5 mL) was refluxed for 72 hrs. Then the solvent was removed, and the residue was chromatographed

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(Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow oil. It was recrystallized from EtOAc and hexane to afford yellow crystals (70 mg, 21%):
5 m. p. 175.5-176.0 °C. Anal. Calcd. for C₃₈H₄₃N₃O₅: C, 73.41, H, 6.97, N, 6.76. Found: C, 73.21, H, 6.81, N, 6.52.

EXAMPLE 26

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1,4-Dihydro-3-methoxycarbonyl-4-(3,4-dimethoxyphenyl)-4-(3,4-Dimethoxyphenyl)-2,6-Dimethyl-5-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (26). This compound was prepared according to Method A. A
15 solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528 mmol), and 3,4-dimethoxybenzaldehyde (87.7 mg, 0.528 mmol) in 1-butanol (5 mL) was refluxed for 84 hrs. Then the solvent was
20 removed, and the residue was chromatographed (Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow oil. It was recrystallized from EtOAc and hexane to afford white crystals (60 mg, 18%): m. p.
25 180.0-181.0 °C. Anal. Calcd. for C₃₈H₄₅N₃O₅: C, 73.17, H, 7.27, N, 6.74. Found: C, 73.21, H, 7.05, N, 6.54.

EXAMPLE 27

30 1,4-Dihydro-3-methoxycarbonyl-4-(3,4,5-trimethoxyphenyl)-2,6-dimethyl-5-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (27). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg,
35 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528 mmol), and 3,4,5-trimethoxybenzaldehyde (103.6 mg, 0.528 mmol) in 1-butanol (5 mL) was refluxed for 84 hrs. Then

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the solvent was removed, and the residue was chromatographed (Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow oil. It was
5 recrystallized from EtOAc and hexane to afford white crystals (70 mg, 20%): m. p. 187.0-188.0 °C. Anal. Calcd. for C₃₉H₄₇N₃O₈: C, 71.65, H, 7.25, N, 6.43. Found: C, 71.65, H, 7.28, N, 6.41.

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EXAMPLE 28

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(3-methyl-4-nitrophenyl)-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (28). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (300 mg, 0.792 mmol), methyl 3-aminocrotonate (94.1 mg, 0.792 mmol), and 3-methyl-4-nitrobenzaldehyde (130.8 mg, 0.792 mmol) in 1-butanol (5 mL) was refluxed for 48 hrs. Then the solvent was removed, and the residue was chromatographed (Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow solid. It was recrystallized from EtOAc and hexane to afford white crystals (130 mg, 29%): m. p. 222.0-222.5 °C. Anal. Calcd. for C₃₇H₄₂N₄O₅: C, 71.36, H, 6.80, N, 8.99. Found: C, 71.00, H, 7.43, N, 8.61.

EXAMPLE 29

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1,4-Dihydro-3-methoxycarbonyl-4-(3-methoxy-4-nitrophenyl)-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (29). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (300 mg, 0.792 mmol), methyl 3-aminocrotonate (94.1 mg, 0.792 mmol), and 3-methoxy-4-nitrobenzaldehyde (143.4 mg, 0.792

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mmol) in 1-butanol (5 mL) was refluxed for 72 hrs. Then the solvent was removed, and the residue was chromatographed (Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a brown oil. It was recrystallized from EtOAc and hexane to afford brown solid (23 mg, 4.5%): m. p. 211.0-213.0 °C. Anal. Calcd. for C₃₇H₄₂N₄O₆: C, 69.57, H, 6.63, N, 8.77. Found: C, 69.37, H, 6.48, N, 8.58.

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EXAMPLE 30

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(3-nitrophenyl)-5-(N-(3-(4-phenylpiperidin-1-yl)propyl)carboxamido)pyridine (30). This compound was prepared according to Method A. A solution of N-(3-(4-phenylpiperidin-1-yl)propyl) acetoacetamide (300 mg, 0.992 mmol), methyl 3-aminocrotonate (117.7 mg, 0.992 mmol), and 3-nitrobenzaldehyde (149.9 mg, 0.992 mmol) in 1-butanol (5 mL) was refluxed for 6 days. Then the solvent was removed, and the residue was chromatographed (Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow oil. It was recrystallized from EtOAc and hexane to afford yellow crystals (91 mg, 17%): m. p. 78.0-80.0 °C. Anal. Calcd. for C₃₀H₃₆N₄O₅: C, 67.65, H, 6.81, N, 10.52. Found: C, 67.93, H, 6.91, N, 10.11.

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EXAMPLE 31

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1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(4-methylphenyl)-5-(N-(3-(4-phenylpiperidin-1-yl)propyl)carboxamido)pyridine (31). This compound was prepared according to Method A. A solution of N-(3-(4-phenylpiperidin-1-yl)propyl) acetoacetamide (300 mg, 0.992 mmol), methyl 3-aminocrotonate (117.7 mg, 0.992 mmol), and p-tolualdehyde (117.0 ul, d 1.019, 0.992 mmol)

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in 1-butanol(5 mL) was refluxed for 72 hrs. Then the solvent was removed, and the residue was chromatographed (Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow oil. It was recrystallized from EtOAc and hexane to afford yellow crystals (79 mg, 16%): m. p. 139.0-139.5 °C. Anal. Calcd. for C₃₁H₃₉N₃O₃: C, 74.22, H, 7.83, N, 8.38. Found: C, 74.19, H, 7.87, N, 8.25.

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EXAMPLE 32

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-5-(N-(3-(4-phenylpiperidin-1-yl)propyl)carboxamido)-4-(4-pyridyl)pyridine (32). This compound was prepared according to Method A. A solution of N-(3-(4-phenylpiperidin-1-yl)propyl) acetoacetamide (300 mg, 0.992 mmol), methyl 3-aminocrotonate (117.7 mg, 0.992 mmol), and 4-pyridinecarboxaldehyde (94.7 ul, d 1.122, 0.992 mmol) in 2-propanol (5 mL) was refluxed for 48 hrs. Then the solvent was removed, and the residue was chromatographed (Flash silica; hexane : EtOAc : Et₃N = 50 : 50 : 3, hexane : EtOAc : Et₃N = 10 : 90 : 6, EtOAc : Et₃N = 10 : 1) to give a yellow oil. It was recrystallized from EtOAc and hexane to afford light yellow crystals (220 mg, 45%): m. p. 79.0-80.0 °C. Anal. Calcd. for C₂₉H₃₆N₄O₃·1/2H₂O: C, 69.99, H, 7.49, N, 11.26. Found: C, 70.18, H, 7.51, N, 11.21.

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EXAMPLE 33

4-(5-Benzofurazanyl)-5-carboxamido-1,4-dihydro-2,6-dimethyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (33). This compound is prepared according to Method A. A mixture of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (1 equivalent), 3-aminocrotonamide (1 equivalent) and 5-

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benzofurazan carboxaldehyde (1 equivalent) in 2-propanol is heated at reflux for several days and then concentrated. After flash chromatography and recrystallization, the product is isolated and characterized spectroscopically.

EXAMPLE 34

4-(4-Acetamidophenyl)-5-carboxamido-1,4-dihydro-2,6-dimethyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (34). This compound is prepared according to Method A. A mixture of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (1 equivalent), 3-aminocrotonamide (1 equivalent) and 4-acetamidobenzaldehyde (1 equivalent) in 2-propanol is heated at reflux for several days and then concentrated. After flash chromatography and recrystallization, the product is isolated and characterized spectroscopically.

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EXAMPLE 35

5-Carboxamido-1,4-dihydro-4-(4-methanesulfonylphenyl)-2,6-dimethyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (35). This compound is prepared according to Method A. A mixture of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (1 equivalent), 3-aminocrotonamide (1 equivalent) and 4-methanesulfonylbenzaldehyde (1 equivalent) in 2-propanol is heated at reflux for several days and then concentrated. After flash chromatography and recrystallization, the product is isolated and characterized spectroscopically.

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EXAMPLE 36

5-Carboxamido-1,4-dihydro-4-(2-hydroxybenzimidazol-5-yl)-

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2,6-dimethyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (36). This compound is prepared according to Method A. A mixture of N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (1
5 equivalent), 3-aminocrotonamide (1 equivalent) and 2-hydroxybenzimidazole-5-carboxaldehyde (1 equivalent) in 2-propanol is heated at reflux for several days and then concentrated. After flash chromatography and recrystallization, the product is isolated and
10 characterized spectroscopically.

EXAMPLE 37

5-Cyano-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-3-{N-
15 [3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (37). This compound was prepared according to Method A. The solution of 3-aminocrotononitrile (67 mg, 0.816 mmol), 4-nitrobenzaldehyde (123 mg, 0.816 mmol) and N-(3-(4,4-diphenylpiperidin-1-yl)propyl)
20 acetoacetamide (309 mg, 0.816 mmol) in 50 mL of 2-propanol was refluxed for 48 hrs. After the solvent was removed, the residue was purified by chromatography (SiO₂, MeOH: CHCl₃, 10:90) to give a yellowish oil, which was converted into the hydrochloride salt and recrystallized
25 from MeOH/Et₂O, 12 mg (2.4% yield) colorless crystals was obtained. M.p. 252 °C (dec); Calcd for C₃₅H₃₇N₅O₃·HCl·1/2H₂O: C 67.68, H 6.33, N 11.27; Found: C 67.63, H 6.29, N 10.88.

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EXAMPLE 38

1,4-Dihydro-2,6-dimethyl-5-(N-methyl)carboxamido-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (38). This compound was
35 prepared according to Method A. The solution of 3-amino-N-methylcrotonamide (60.3 mg, 0.528 mmol), 4-nitrobenzaldehyde (79.8 mg, 0.528 mmol) and N-(3-(4,4-

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diphenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.528 mmol) in 50 mL of 2-propanol was refluxed for 48 hrs. After the solvent was removed, the residue was purified by chromatography (SiO_2 , MeOH: CHCl_3 , 10:90) to give a yellowish oil, which was precipitated from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to afford 38 mg (7.1% yield) of yellowish powder: m.p. 134 °C; Calcd for $\text{C}_{36}\text{H}_{41}\text{N}_5\text{O}_4 \cdot 1/4\text{H}_2\text{O}$: C 70.62, H 6.83, N 11.44, Found: C 70.77, H 6.56, N 10.95.

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EXAMPLE 39

1,4-Dihydro-2,6-dimethyl-3-(N,N-dimethyl)carboxamido-4-(4-nitrophenyl)-5-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (39). This compound was prepared according to Method A. The solution of 3-amino-N,N-dimethylcrotonamide (76 mg, 0.592 mmol), 4-nitrobenzaldehyde (89 mg, 0.592 mmol) and N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (224 mg, 0.592 mmol) in 50 mL of 2-propanol was refluxed for 48 hrs. After the solvent was removed, the residue was purified by chromatography (SiO_2 , MeOH: CHCl_3 , 10:90) to give a yellowish oil, which was precipitated by AcOEt/hexane mixture to afford 30 mg (8.0% yield) of yellowish powder: M.p. 135 °C; Calcd for $\text{C}_{37}\text{H}_{43}\text{N}_5\text{O}_4 \cdot 1/2\text{H}_2\text{O}$: C 70.45, H 7.03, N 11.10, Found: C 70.51, H 6.89, N 11.13.

EXAMPLE 40

1,4,5,6,7,8-Hexahydro-2-methyl-4-(4-nitrophenyl)-5-oxo-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidoquinoline (40). This compound was prepared according to Method A. The solution of 3-amino-2-cyclohexene-1-one (335 mg, 3.00 mmol), 4-nitrobenzaldehyde (445 mg, 3.00 mmol) and N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (113 mg, 3.00 mmol) in 100 mL of 2-propanol was refluxed for 72

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hrs. After the solvent was removed, the residue was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3$, 10:90) to give a yellowish oil, which was precipitated from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to afford 127 mg (7.0% yield) of yellow powder:

5 M.p. 143-146 °C; Calcd for $\text{C}_{37}\text{H}_{40}\text{N}_4\text{O}_4 \cdot 1/2\text{H}_2\text{O}$: C 72.41, H 6.73, N 9.13; Found: C 72.69, H 6.66, N 8.98.

EXAMPLE 41

10 3-Carboxamido-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (41). This compound was prepared according to Method A. The solution of 3-amino-2-pentenamide (219 mg, 1.91 mmol), 4-nitrobenzaldehyde

15 (289 mg, 1.91 mmol) and N-(3-(4,4-diphenylpiperidin-1-yl)propyl) acetoacetamide (667 mg, 1.91 mmol) in 50 mL of 2-propanol was refluxed for 72 hrs. After the solvent was removed, the residue was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3$, 10:90) to give a yellowish oil, which

20 was precipitated from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to afford 156 mg (13.3% yield) of yellowish powder: M.p. 120-124 °C; Calcd for $\text{C}_{36}\text{H}_{41}\text{N}_5\text{O}_4 \cdot 1/4\text{H}_2\text{O}$: C 70.62, H 6.83, N 11.44; Found: C 70.91, H 6.98, N 10.97.

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EXAMPLE 42

5-Carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (42). This compound was prepared according to Method A. To 30 mL of boiling p-xylene was added a solution of 6-ethyl-2,2-dimethyl-2H,4H-1,3-dioxin-4-one (760 mg, 5 mmol) and 3-(4,4-diphenylpiperidin-1-yl)propylamine (1.48 g, 5 mmol) in 20 mL p-xylene dropwise in about 15 min., during which time,

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35 about 20 mL of xylene was distilled off through a condenser. Heating was continued for an additional 45 min. to distill most of the xylene. The remaining xylene

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was further removed by evaporation in vacuo. The product, propionylacetic acid N-[3-(4,4-diphenylpiperidin-1-yl)propyl]amide, was used for next reaction without further purification.

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A solution of 3-amino-2-pentenamide (261 mg, 2.28 mmol), 4-nitrobenzaldehyde (345 mg, 2.28 mmol) and propionylacetic acid N-[3-(4,4-diphenylpiperidin-1-yl)propyl]amide (896 mg, 2.28 mmol) in 50 mL of EtOH was
10 refluxed for 72 hrs. After the solvent was removed, the residue was purified by chromatography (SiO₂, MeOH: CHCl₃, 10:90) to give a yellowish oil, which was precipitated from CH₂Cl₂/Et₂O to afford 81 mg (5.4% yield) of yellowish powder: M.p. 119-123 °C; Calcd for C₃₇H₄₃N₃O₄·3/2H₂O: C
15 68.02, H 7.17, N 10.72; Found: C 68.05, H 6.71, N 10.89.

EXAMPLE 43

2-(Furan-3-yl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-
20 (4-nitrophenyl)-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carbamidopyridino, Hydrochloride Salt (43). This compound was initially prepared according to Method A, and later according to Method B (see below). Method
A: A stirred solution of 191 mg of 1-(3-aminopropyl)-
25 4,4-diphenylpiperidine (0.676 mmol), 123 mg of ethyl 3-oxo-3-(furan-3-yl)propionate (0.676 mmol), and 83 mg of dimethylaminopyridine (0.676 mmol) in 5 mL of dry toluene were heated at reflux temperature for 18 hrs, cooled, and the residue was dissolved in 30 mL of EtOAc. The
30 resulting solution was extracted with 2 X 20 mL of aqueous 1 N HCl solution. The combined aqueous extracts were washed with 20 mL of 1:1 EtOAc-ether, basified with NaHCO₃ (pH = 8-9), and extracted with 2 X 20 mL of EtOAc. The combined EtOAc extracts were dried (Na₂SO₄), the
35 solvent was removed in vacuo, and the crude product was chromatographed on 100 g of silica packed with MeOH-isopropyl amine-EtOAc (1:1:98). The column was eluted

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with MeOH-isopropyl amine-EtOAc 1:1:98, 2:1:97, 5:1:94, 10:1:89, 20:1:79 (0.5 L each) to give N-(3-(4,4-diphenylpiperidin-1-yl)propyl 3-oxo-3-(furan-3-yl)propanamide as a slightly yellow viscous oil. The product was used in the next step after spectral characterization.

A mixture of 40 mg of N-(3-(4,4-diphenylpiperidin-1-yl)propyl 3-oxo-3-(furan-3-yl)propanamide (0.096 mmol), 11 mg of methyl 3-aminocrotonate (0.096 mmol), and 15 mg of 4-nitrobenzaldehyde (0.096 mmol) in 5 mL of isopropanol was heated at reflux temperature for 4 days, cooled, and the solvent was removed in vacuo. The crude product was applied to a preparative Thin Layer Chromatography (TLC) plate and eluted with 5% MeOH-EtOAc. A yellow band was collected. This crude product was dissolved in a minimum of EtOAc (0.5 mL) and excess HCl in ether (1 mL) was added to afford, after filtration, 5.8 mg (1% from ethyl 3-oxo-3-(furan-3-yl)propionate) of the free base as a yellow powder: mp 197-205 °C (decomp.). Anal. Calcd for $C_{35}H_{40}N_4O_6 \cdot HCl$: C, 66.61; H, 6.03; N, 8.18. Found: C, 66.61; H, 5.81; N, 7.94.

Method B: A mixture of 894 mg of ethyl 3-(furan-3-yl)-3-oxopropionate (4.90 mmol) and 347 mg of 3-hydroxypropionitrile (4.88 mmol) was heated in an oil bath to 180-205 °C for 0.5 hrs. The reaction mixture was cooled and distilled under reduced pressure. Three fractions were obtained. ¹H NMR indicated that the third fraction (bp 100-140 °C (0.5 mm Hg)) was a 1:1 mixture of ethyl 3-(furan-3-yl)-3-oxopropionate and 2-cyanoethyl 3-(furan-3-yl)-3-oxopropionate. This mixture was used in the condensation step after spectral characterization.

A solution of the 3-oxoesters (approximately 1.67 mmol), 192 mg of methyl 3-aminocrotonate (1.67 mmol), and 252 mg of 4-nitrobenzaldehyde (1.67 mmol) in 5 mL of isopropanol

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was heated at reflux temperature for 30 hrs, cooled, and the solvent was removed in vacuo. The residue was dissolved in 15 mL of dioxane and 15 mL of water (containing 35 mg of NaOH), stirred for 0.5 hr, and concentrated in vacuo. The residue was partitioned between ethyl acetate and water (20 mL each), separated, and the aqueous extract was washed with ethyl acetate (2 X 20 mL). The organic solutions were discarded. The aqueous extract was acidified with concentrated HCl (pH = 3), and the resulting cloudy mixture was extracted with ethyl acetate (2 X 30 mL). The combined organic extracts were dried (Na_2SO_4), and the solvent was removed in vacuo to give 2-(furan-3-yl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid as a yellow oil that partially solidified under reduced pressure. A solution of 75 mg of 2-(furan-3-yl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (0.20 mmol) and 35 mg of carbonyldiimidazole (0.22 mmol) was stirred at room temperature for 1 hr. The solvent was removed in vacuo, and the crude product was chromatographed on 100 g of silica packed with 2% MeOH-EtOAc. The column was eluted with 3% MeOH-EtOAc to give 45 mg (58%) of 5-carboxamido-2-(furan-3-yl)-1,4-dihydro-3-(imidazol-1-yl)carbonyl-6-methyl-4-(4-nitro)phenylpyridine.

5-Carboxamido-2-(furan-3-yl)-1,4-dihydro-3-(imidazol-1-yl)carbonyl-6-methyl-4-(4-nitro)phenylpyridine was dissolved in 5 mL of dry THF and excess (1.5 equivalents) of 1-(3-aminopropyl)-4,4-diphenylpiperidine was added to the reaction mixture. The resulting mixture was heated at reflux temperature for 3 hrs and cooled to room temperature. The solvent was removed in vacuo, and the residue was dissolved in 20 mL of ethyl acetate and washed with water (3 X 10 mL). After removal of the solvent, the crude product was chromatographed on 50 g of silica packed with 10% MeOH-EtOAc. The column was eluted

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with 10% MeOH-EtOAc to give 61 mg of 2-(furan-3-yl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamido-pyridine, which was spectroscopically identical to the product obtained by Method A.

EXAMPLE 44

Acetoacetic acid 3-(N,N-dimethyl)aminopropyl ester.

10 Diketene (2.54 mL, 33.0 mmol, 1.30 equiv) was added to a solution of 3-(N,N-dimethyl)aminopropan-1-ol (3.00 mL, 25.4 mmol, 1.00 equiv, Aldrich) in toluene (30 mL) and the mixture was stirred at room temperature for 70 hours. The solvent was removed to afford 4.76 g of brown oil, 15 which was characterized spectroscopically and used for the next reaction without purification.

1,4-Dihydro-5-methoxycarbonyl-2,6-dimethyl-3-{3-[(N,N-dimethyl)amino]propoxy}carbonyl-4-(4-nitrophenyl)pyridine hydrochloride (44). This compound was prepared according to Method A. A mixture of acetoacetic acid 3-(N,N-dimethyl)aminopropyl ester (0.937 g, 5.00 mmol, 1.00 equiv), methyl-3-aminocrotonate (576 mg, 5.00 mmol, 1.00 equiv) and 4-nitrobenzaldehyde (756 mg, 5.00 mmol, 1.00 equiv) in 2-propanol (30 mL) was stirred at reflux for 60 hours. After removal of the solvent, the residue was purified twice by flash chromatography on SiO₂ (1. EtOAc-MeOH 1:0 to 6:1; 2. CH₂Cl₂-isopropylamine 10:0.5) to give 888 mg of yellow solid, which was characterized spectroscopically. To a solution of this product in CH₂Cl₂ (10 mL) was added a solution of HCl in ether (1.0 M, 2.50 mL, 2.5 mmol, 1.2 equiv). After removal of the solvents, a solution of the residue in CH₂Cl₂ (5 mL) was added dropwise with swirling to 20 mL of ether. 35 Filtration afforded 516 mg of yellow solid: m.p. 120-121 °C; Anal. Calcd. for C₂₁H₂₇N₃O₆·HCl: C, 55.57; H, 6.22; N, 9.26. Found: C, 55.29 H, 6.50; N, 8.55.

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EXAMPLE 45

(±)-1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophenyl)-5-{N-[3-(4-phenylpiperidin-1-yl)propyl]}carboxamidopyridine hydrochloride hemihydrate ((±)-45). This compound was prepared according to Method A. A solution of N-(3-(4-phenylpiperidin-1-yl)propyl)acetoacetamide (4.50 g, 14.2 mmol, 1.00 equiv), methyl 3-aminocrotonate (1.68 g, 14.2 mmol, 1.00 equiv), and 4-nitrobenzaldehyde (2.15 g, 14.2 mmol, 1.00 equiv) in 2-propanol was stirred at reflux for 52 hours under argon. After removal of the solvent, the residue was purified by flash chromatography (SiO₂, EtOAc-MeOH-Et₃N 9:1:0 to 6:1:0.1). A solution of the chromatographed product in CH₂Cl₂ (15 mL) was added dropwise with swirling to 250 mL of ether-hexane (1:1). Filtration of this mixture afforded 2.50 g (33%) of yellow crystalline solid, which was characterized spectroscopically. To a solution of this product (1.0 g, 1.9 mmol, 1.0 equiv) in CH₂Cl₂ (10 mL) was added dropwise a solution of HCl in ether (1.0 M, 2.3 mL, 2.3 mmol, 1.2 equiv). After removal of the solvents, a solution of the residue in CH₂Cl₂ (10 mL) was added dropwise to 70 mL of ether with swirling. Filtration afforded 1.04 g of yellow solid: m.p. 159-160 °C; Anal. Calcd. for C₃₀H₃₆N₄O₅·HCl·0.5 H₂O: C, 62.33; H, 6.63; N, 9.69. Found: C, 62.19; H, 6.38; N, 9.34.

(-)- and (+)-45 hydrochloride hemihydrate. The enantiomers of 45 free base were separated on a chiral HPLC column as follows. Three injections of (±)-45 free base (ca. 25 mg per injection in EtOH solution) were made onto a Chiralpak AS column (20 x 250 mm) which was pre-equilibrated with EtOH-hexane-diethylamine (10:90:0.017). The column was eluted with a gradient at 9.0 mL/min: hexane, 0.0-3.0 min; ramp to EtOH-hexane-diethylamine (30:70:0.05) 3.0-6.0 min and hold at final conditions.

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Detection was by UV absorption at 300 nm. The first major peak eluted at 19.56 min. To a solution of this product in CH_2Cl_2 (3 mL) was added HCl in ether (1.0 M, 0.25 mL). After removal of the solvents, a solution of the residue in CH_2Cl_2 (2 mL) was added dropwise into ether (6 mL) with swirling to give, after filtration, 19.4 mg of yellow powder: $[\alpha]_D = -18.4^\circ$ (EtOH, 0.000711 g/mL); m.p. 160 °C; Anal. Calcd. for $\text{C}_{30}\text{H}_{34}\text{N}_4\text{O}_5 \cdot \text{HCl} \cdot 0.5 \text{H}_2\text{O}$: C, 62.33; H, 6.63; N, 9.69. Found: C, 62.74; H, 6.73; N, 9.66. The second major peak, which eluted at 29.28 min, was converted to the HCl salt and precipitated as described for the (-)- enantiomer to afford 20.6 mg of yellow powder: $[\alpha]_D = +24.4^\circ$ (EtOH, 0.000753 g/mL); m.p. 161 °C; Anal. Calcd. for $\text{C}_{30}\text{H}_{34}\text{N}_4\text{O}_5 \cdot \text{HCl} \cdot \text{H}_2\text{O}$: C, 62.33; H, 6.63; N, 9.69. Found: C, 62.33; H, 6.26; N, 9.51.

EXAMPLE 46

1-[3-(N-Methylamino)propyl]-4,4-diphenylpiperidino. To a stirred solution of 3-(4,4-diphenylpiperidin-1-yl)propionitrile (5.00 g, 17.2 mmol, 1.00 equiv) in CH_2Cl_2 (40 mL) was added HCl in ether (1.0 M, 22.4 mL, 22 mmol, 1.3 equiv). After removal of the solvents, the residue and trimethyloxonium tetrafluoroborate (9.67 g, 65.4 mmol, 3.80 equiv) were stirred in refluxing anhydrous CH_2Cl_2 (80 mL) under argon for 44 hours. The mixture was cooled to 0 °C, anhydrous MeOH (5 mL) was added, and stirring was continued for 1 hour at 0 °C. The solvents were removed and the residue was dissolved in anhydrous MeOH (30 mL). Sodium borohydride (5.20 g, 138 mmol, 8.00 equiv) was added at 0 °C, and stirring was continued at this temperature under argon for 2 hours. The solution was acidified to pH 1 by slow addition of 6 N aqueous HCl (40 mL) at 0 °C and stirred for 3 hours at room temperature. After removal of the solvents, water (30 mL) was added and the mixture was basified to pH 9 by addition of 6 N aqueous NaOH. The mixture was extracted with CH_2Cl_2 .

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(3 x 100 mL), and the combined organic solutions were dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , EtOAc-MeOH-isopropylamine 9:1:0 to 5:1:0.2) to give 2.18 g (41%) of yellow solid, which was characterized spectroscopically.

N-[3-(4,4-Diphenylpiperidin-1-yl)propyl]-*N*-methylethanacetamide. Diketene (0.98 mL, 12.7 mmol, 1.50 equiv) was added at 0 °C to a stirred solution of 1-[3-(*N*-methylamino)propyl]-4,4-diphenylpiperidine (2.61 g, 8.46 mmol, 1.00 equiv) in anhydrous toluene (30 mL) under argon, and stirring was continued for 1 hour. After removal of the solvent, the residue was purified by flash chromatography (SiO_2 , EtOAc-MeOH-isopropylamine 9:1:0 to 6:1:0.1) to afford 2.97 g (89%) of brown oil, which was characterized spectroscopically.

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-5-([*N*-[3-(4,4-diphenylpiperidin-1-yl)propyl])carboxamide-4-(4-nitrophenyl)pyridine hydrochloride hemihydrate (46). This compound was prepared according to Method A. A solution of *N*-[3-(4,4-diphenylpiperidin-1-yl)propyl]-*N*-methylacetamide (1.49 g, 3.79 mmol, 1.00 equiv), methyl 3-aminocrotonate (479 mg, 4.16 mmol, 1.10 equiv), and 4-nitrobenzaldehyde (629 mg, 4.16 mmol, 1.10 equiv) in isopropanol (20 mL) was stirred at room temperature for 0.5 hour and then refluxed under argon for 60 hours. The mixture was cooled to room temperature and concentrated, and the residue was purified three times by flash chromatography on SiO_2 (1. EtOAc-MeOH 10:0 to 9:1; 2. CH_2Cl_2 -Et₃N 96:4; 3. EtOAc-MeOH 19:1) to afford 210 mg of light yellow solid, which was characterized spectroscopically. To a solution of this product (190 mg, 0.305 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added HCl in ether (1.0 M, 0.37 mL, 0.37 mmol, 1.2 equiv) with swirling. After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to 20 mL of

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ether with swirling. Filtration afforded 196 mg of yellow solid: m.p. 179-180 °C; Anal. Calcd. for $C_{37}H_{43}N_4O_5 \cdot HCl \cdot 0.5 H_2O$: C, 66.51; H, 6.64; N, 8.38. Found: C, 66.32; H, 6.58; N, 8.16.

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EXAMPLE 47

4-Aminopent-3-en-2-one. Concentrated ammonium hydroxide (ca. 14.8 M, 6.6 mL, 98 mmol, 1.0 equiv) was added dropwise to neat 2,4-pentanedione (10 mL, 97 mmol, 1.0 equiv) at ambient temperature. Water (5 mL) was added and the mixture was stirred for 1 hour. The solvent was removed to give 9.2 g (95%) of white solid, which was characterized spectroscopically and used for the next step without purification.

5-Acetyl-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamido-pyridine (47). This compound was prepared according to Method A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl)acetoacetamide (7.57 g, 20.0 mmol, 1.00 equiv), 4-aminopent-3-en-2-one (2.18 g, 22.0 mmol, 1.10 equiv), and 4-nitrobenzaldehyde (3.33 g, 22.0 mmol, 1.10 equiv) in isopropanol (30 mL) was refluxed under argon for 72 hours. The mixture was cooled to room temperature and concentrated. The residue was purified on two successive SiO_2 flash chromatography columns (1. EtOAc, followed by EtOAc-MeOH 19:1; 2. CH_2Cl_2 -MeOH 96:4) to give 3.5 g of yellow solid. A solution of this product in CH_2Cl_2 was added dropwise to EtOAc at room temperature. Storage of the resulting mixture at -10 °C for 12 hours, followed by filtration and washing with CH_2Cl_2 -EtOAc (1:1), afforded 2.10 g of yellow solid (18%), which was characterized spectroscopically. To a solution of this product (50 mg, 0.084 mmol, 1.0 equiv) in CH_2Cl_2 -EtOH (1:1, 10 mL) was added HCl in ether (1.0 M, 0.13 mL, 0.13 mmol, 1.5 equiv) with swirling. After removal of the solvents, the

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residue was dissolved in CH_2Cl_2 -EtOH 1:1 (3 mL) and added dropwise to 20 mL of ether-hexane (1:1). Filtration afforded 41 mg of yellow solid: m.p. 173-174 °C; Anal. Calcd. for $\text{C}_{36}\text{H}_{40}\text{N}_4\text{O}_4 \cdot \text{HCl} \cdot \text{H}_2\text{O}$: C, 66.81; H, 6.70; N, 8.66.

5 Found: C, 66.44; H, 6.34; N, 8.43.

EXAMPLE 48

1-(3-Hydroxypropyl)-4-phenylpiperidine. A suspension of
10 4-phenylpiperidine (3.00 g, 18.6 mmol, 1.00 equiv), 3-bromopropan-1-ol (2.12 mL, 22.3 mmol, 1.20 equiv), potassium carbonate (12.8 g, 93.0 mmol, 5.00 equiv), and potassium iodide (124 mg, 0.74 mmol, 0.04 equiv) in n-butan-
15 ol (50 mL) and 1,4-dioxane (50 mL) was stirred at reflux under argon for 48 hours. The mixture was cooled to room temperature and concentrated. Water (50 mL) was added and the mixture was extracted with CH_2Cl_2 (4 x 100 mL). The combined organic solutions were dried over MgSO_4 and concentrated. The residue was crystallized from
20 ethyl acetate to give 3.36 g (82%) of tan solid, which was characterized spectroscopically.

3-(4-Phenylpiperidin-1-yl)propyl acetoacetate. Diketene (0.95 mL, 12 mmol, 1.3 equiv) was added to a solution of
25 1-(3-hydroxypropyl)-4-phenylpiperidine (2.08 g, 9.48 mmol, 1.0 equiv) in toluene (30 mL), and the mixture was stirred under argon for 70 hours at room temperature. Removal of solvent gave 2.88 g (100%) of light brown, viscous oil, which was characterized spectroscopically
30 and used for the next reaction without purification.

1,4-Dihydro-5-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophenyl)-3-[3-(4-phenylpiperidin-1-yl)propoxy]carbonylpyridine hydrochloride hydrate
35 (48). This compound was prepared according to Method A. 3-(4-Phenylpiperidin-1-yl)propyl acetoacetate (2.85 g, 9.40 mmol, 1.00 equiv), methyl 3-aminocrotonate (1.08 g,

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9.40 mmol, 1.00 equiv) and 4-nitrobenzaldehyde (1.42 g, 9.40 mmol, 1.00 equiv) were stirred together in 2-propanol (50 mL) at reflux for 48 hours under argon. After removal of the solvent, the residue was purified by
5 flash chromatography (SiO_2 , Et_2O -hexane 1:1, followed by EtOAc-hexane 2:1 to 1:0) to give 1.76 g (35%) of yellow solid, which was characterized spectroscopically. This product was dissolved in CH_2Cl_2 (10 mL) and a solution of HCl in ether (1.0 M, 4.5 mL, 1.4 equiv) was added. After
10 removal of the solvents, the residue was dissolved in CH_2Cl_2 (10 mL) and added dropwise to ether (50 mL) with swirling to give, after filtration, 1.75 g of yellow solid: m.p. 139-140°C; Anal. Calcd. for $\text{C}_{30}\text{H}_{35}\text{N}_3\text{O}_6 \cdot \text{HCl}$: C, 63.20; H, 6.37; N, 7.37. Found: C, 63.05; H, 6.56; N,
15 7.16.

EXAMPLE 49

5-Acetyl-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-3-[3-
20 (4,4-diphenylpiperidin-1-yl)propoxy]carbonylpyridine hydrochloride hemihydrate (49). This compound was prepared according to Method A. A mixture of 4-aminopent-3-en-2-one (287 mg, 2.90 mmol, 1.00 equiv), 4-nitrobenzaldehyde (438 mg, 2.90 mmol, 1.00 equiv), and 3-
25 (4-phenylpiperidin-1-yl)propyl acetoacetate (1.10 g, 2.90 mmol, 1.00 equiv) in isopropanol (30 mL) was stirred at reflux under argon for 60 hours. After removal of the solvent, the residue was purified by flash chromatography (SiO_2 , EtOAc-hexane 1:1 to 1:0) to give 371 mg (22%) of
30 yellow solid, which was characterized spectroscopically. This product was dissolved in CH_2Cl_2 (5 mL) and a solution of HCl in ether (1.0 M, 1.0 mL, 1.6 equiv) was added. After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (20 mL) with
35 swirling to give, after filtration, 319 mg of yellow solid: m.p. 160.0-160.5 °C; Anal. Calcd. for $\text{C}_{38}\text{H}_{39}\text{N}_3\text{O}_5 \cdot \text{HCl} \cdot 0.5 \text{H}_2\text{O}$: C, 67.75; H, 6.32; N, 6.58. Found:

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C, 67.62 H, 6.34; N, 6.28.

EXAMPLE 50

- 5 3-(Piperidin-1-yl)propyl acetoacetate. Diketene (1.48 mL, 19.2 mmol, 1.30 equiv) was added to a solution of 1-(3-hydroxypropyl)piperidine (2.12 g, 14.8 mmol, 1.00 equiv, Leonard, N. J.; Musker, W. K. J. Am. Chem. Soc. 1960, 82, 5148) in toluene (30 mL), and the mixture was
- 10 stirred under argon for 72 hours at room temperature. Removal of solvent gave 3.52 g (100%) of light brown, viscous oil, which was characterized spectroscopically and used for the next reaction without purification.
- 15 1,4-Dihydro-5-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophenyl)-3-[3-(piperidin-1-yl)propoxy]carbonylpyridine hydrochloride etherate (50). This compound was prepared according to Method A. 3-(Piperidin-1-yl)propyl acetoacetate (2.20 g, 9.68 mmol, 1.00 equiv), methyl 3-
- 20 aminocrotonate (1.11 g, 9.68 mmol, 1.00 equiv) and 4-nitrobenzaldehyde (1.46 g, 9.68 mmol, 1.00 equiv) were stirred together in 2-propanol (50 mL) at reflux for 72 hours under argon. After removal of the solvent, the residue was purified by flash chromatography (SiO₂, MeOH-EtOAc 0:1 to 1:19) to give 1.71 g (39%) of yellow solid, which was characterized spectroscopically. This product
- 25 was dissolved in CH₂Cl₂ (15 mL) and a solution of HCl in ether (1.0 M, 4.5 mL, 1.2 equiv) was added. After removal of the solvents, the residue was dissolved in
- 30 CH₂Cl₂ (10 mL) and added dropwise to ether (70 mL) with swirling to give, after filtration, 1.78 g of yellow solid: m.p. 128-129 °C; Anal. Calcd. for C₂₄H₃₁N₃O₆·HCl·0.4 Et₂O: C, 58.72; H, 6.93; N, 8.02. Found: C, 58.44 H, 6.82; N, 7.76.

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EXAMPLE 51

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N-(3-(Piperidin-1-yl)propyl)acetoacetamido. Diketene (2.40 mL, 31.1 mmol, 1.50 equiv) was added at 0 °C to a stirred solution of 1-(3-aminopropyl)piperidine (2.95 g, 20.7 mmol, 1.0 equiv, Bates, R. J.; Cymerman-Craig, J.; Moyle, M.; Yong, R. J. *J. Chem. Soc.* 1956, 388) in anhydrous THF (40 mL) under argon, and stirring was continued at room temperature for 1.5 hours. The mixture was concentrated to give 4.8 g (100%) of light brown oil, which was characterized spectroscopically and used for the next reaction without purification.

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophenyl)-5-{*N*-[3-(piperidin-1-yl)propyl]}carbamidopyridine hydrochloride octahydrate (51). This compound was prepared according to Method A. *N*-(3-(Piperidin-1-yl)propyl)acetoacetamide (4.53 g, 20.0 mmol, 1.00 equiv), methyl 3-aminocrotonate (2.37 g, 20.0 mmol, 1.00 equiv) and 4-nitrobenzaldehyde (3.02 g, 20.0 mmol, 1.00 equiv) were stirred together in 2-propanol (60 mL) at reflux for 60 hours under argon. After removal of the solvent, the residue was purified by flash chromatography (SiO₂, MeOH-EtOAc 0:1 to 1:6) to afford 2.25 g of yellow solid. A solution of this product in CH₂Cl₂ (10 mL) was added dropwise into ether (50 mL) with swirling. A yellow solid (1.75 g, 19%) was collected by filtration and characterized spectroscopically. This product (1.4 g) was dissolved in CH₂Cl₂ (10 mL) and a solution of HCl in ether (1.0 M, 4.5 mL, 1.5 equiv) was added. After removal of the solvents, the residue was dissolved in CH₂Cl₂ (10 mL) and added dropwise to ether (80 mL) with swirling to give, after filtration, 1.38 g of yellow solid: m.p. 150.0-150.5 °C; Anal. Calcd. for C₂₆H₃₂N₄O₅·HCl·0.2 Et₂O: C, 58.66; H, 6.95; N, 11.03. Found: C, 58.31 H, 7.05; N, 10.70.

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EXAMPLE 52

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(4,4-Diphenylpiperidin-1-yl)acetonitrile. A suspension of 4,4-diphenylpiperidine (4.00 g, 16.9 mmol, 1.00 equiv), chloroacetonitrile (1.40 mL, 21.9 mmol, 1.30 equiv, Aldrich), potassium carbonate (4.67 g, 33.8 mmol, 2.00 equiv), and potassium iodide (561 mg, 3.38 mmol, 0.20 equiv) in n-butanol (20 mL) and 1,4-dioxane (20 mL) was stirred at reflux under argon for 48 hours. The mixture was cooled to room temperature and concentrated. The residue was purified by flash chromatography (SiO₂, EtOAc) to afford 4.01 g (86%) of white solid, which was characterized spectroscopically.

1-(2-Aminoethyl)-4,4-diphenylpiperidine. To a stirred solution of (4,4-diphenylpiperidin-1-yl)acetonitrile (3.90 g, 14.1 mmol, 1.0 equiv) in anhydrous THF (10 mL) under argon was added a solution of BH₃ in THF (1.0 M, 50 mL, 50 mmol, 3.5 equiv) at room temperature. The mixture was refluxed for 4.5 hours and then cooled to room temperature and concentrated to a volume of about 30 mL. Aqueous HCl (6 N, 50 mL) was added cautiously and stirring was continued for 2 hours at 50 °C. The mixture was cooled to room temperature, basified to pH 10 by addition of 6 N aq. NaOH, and extracted with CH₂Cl₂ (3 x 100 mL). The combined organic solutions were dried over MgSO₄ and concentrated. To a solution of the residue in CH₂Cl₂ (30 mL) was added HCl in ether (1.0 M, 16 mL, 1.1 equiv). After removal of the solvents, the residue was dissolved in CH₂Cl₂ (10 mL) and this solution was added dropwise into ether (100 mL) with swirling. The resulting solid was filtered and washed with ether (3 x 50 mL). This solid was taken up in water (20 mL), which was basified to pH 10 by addition of 1 M aqueous NaOH, and extracted with CH₂Cl₂ (3 x 50 mL). The combined organic solutions were dried over MgSO₄ and concentrated to give 3.70 g (94%) of white solid, which was characterized spectroscopically.

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N-(2-(4,4-Diphenylpiperidin-1-yl)ethyl)acetoacetamide. Diketene (1.50 mL, 19.2 mmol, 1.50 equiv) was added at 0 °C to a stirred solution of 1-(2-aminoethyl)-4,4-diphenylpiperidine (3.60 g, 12.8 mmol, 1.00 equiv) in anhydrous THF (40 mL) under argon, and stirring was continued at room temperature for 1 hour. The mixture was concentrated to give 4.10 g (88%) of white solid, which was characterized spectroscopically and used for the next reaction without purification.

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1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophenyl)-5-{*N*-(2-(4,4-diphenylpiperidin-1-yl)ethyl)}carbamidopyridine hydrochloride monohydrate (52). This compound was prepared according to Method A. *N*-(2-(4,4-Diphenylpiperidin-1-yl)ethyl)acetoacetamide (2.34 g, 6.41 mmol, 1.00 equiv), methyl 3-aminocrotonate (0.839 g, 7.06 mmol, 1.10 equiv) and 4-nitrobenzaldehyde (1.07 g, 7.06 mmol, 1.10 equiv) were stirred together in 2-propanol (40 mL) at reflux for 68 hours under argon. After removal of the solvent, the residue was purified by flash chromatography (SiO₂, MeOH-EtOAc 0:1 to 1:9) to afford 1.40 g (37%) of yellow solid, which was characterized spectroscopically. This product (1.36 g) was dissolved in CH₂Cl₂ (10 mL) and a solution of HCl in ether (1.0 M, 3.5 mL, 1.5 equiv) was added. After removal of the solvents, the residue was dissolved in CH₂Cl₂ (10 mL) and added dropwise to ether (80 mL) with swirling to give, after filtration, 1.14 g of yellow solid: m.p. 170-171 °C; Anal. Calcd. for C₃₃H₂₉N₄O₅·HCl·0.5 H₂O: C, 65.67; H, 6.30; N, 8.75. Found: C, 65.67; H, 6.35; N, 8.62.

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EXAMPLE 53

4-(4,4-Diphenylpiperidin-1-yl)butyronitrile. A suspension of 4,4-diphenylpiperidine (4.15 g, 17.5 mmol, 1.00 equiv), 4-bromobutyronitrile (2.10 mL, 21.0 mmol, 1.20 equiv, Aldrich), potassium carbonate (4.85 g, 35.0

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mmol, 2.00 equiv), and potassium iodide (581 mg, 3.50 mmol, 0.20 equiv) in n-butanol (20 mL) and 1,4-dioxane (20 mL) was stirred at reflux under argon for 48 hours. The mixture was cooled to room temperature and concentrated. Water (50 mL) was added and the mixture was extracted with CH₂Cl₂ (4 x 150 mL). The combined organic solutions were dried over MgSO₄ and concentrated. The residue was purified by flash chromatography (SiO₂, EtOAc) to afford 4.65 g (87%) of white solid, which was characterized spectroscopically.

1-(4-Aminebutyl)-4,4-diphenylpiperidine. To a stirred solution of 4-(4,4-diphenylpiperidin-1-yl)butyronitrile (4.65 g, 15.3 mmol, 1.0 equiv) in anhydrous THF (20 mL) under argon was added a solution of BH₃ in THF (1.0 M, 54 mL, 54 mmol, 3.5 equiv) at room temperature. The mixture was refluxed for 4.5 hours and then cooled to room temperature and concentrated to a volume of about 40 mL. Aqueous HCl (6 N, 55 mL) was added cautiously at 0 °C and stirring was continued for 2 hours at 55-65 °C. The mixture was cooled to 0 °C, basified to pH 10 by addition of 6 N aq. NaOH, and extracted with CH₂Cl₂ (3 x 100 mL). The combined organic solutions were dried over MgSO₄ and concentrated. To a solution of the residue in CH₂Cl₂ (50 mL) was added HCl in ether (1.0 M, 30 mL, 2.0 equiv). After removal of the solvents, the residue was dissolved in CH₂Cl₂ (10 mL) and this solution was added dropwise into ether (150 mL) with swirling. The resulting solid was filtered and washed with ether (100 mL). This solid was taken up in water (30 mL), which was basified to pH 10 by addition of 1 M aqueous NaOH, and extracted with CH₂Cl₂ (3 x 50 mL). The combined organic solutions were dried over MgSO₄ and concentrated to give 4.51 g (95%) of light brown oil, which was characterized spectroscopically.

N-(4-(4,4-Diphenylpiperidin-1-yl)butyl)acetoneamide.

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Diketene (1.68 mL, 21.9 mmol, 1.50 equiv) was added at 0 °C to a stirred solution of 1-(4-aminobutyl)-4,4-diphenylpiperidine (4.50 g, 14.6 mmol, 1.00 equiv) in anhydrous THF (40 mL) under argon, and stirring was continued at room temperature for 1.5 hours. The mixture was concentrated and the residual oil washed with hexane (3 x 50 mL) to give 5.17 g (90%) of light yellow oil, which was characterized spectroscopically and used for the next reaction without purification.

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophenyl)-5-{N-[4-(4,4-diphenylpiperidin-1-yl)butyl]}carboxamidopyridine hydrochloride hydrate (53). This compound was prepared according to Method A. N-(4-(4,4-diphenylpiperidin-1-yl)butyl)acetoacetamide (2.86 g, 7.30 mmol, 1.00 equiv), methyl 3-aminocrotonate (0.953 g, 8.03 mmol, 1.10 equiv) and 4-nitrobenzaldehyde (1.21 g, 8.03 mmol, 1.10 equiv) were stirred together in 2-propanol (50 mL) at reflux for 72 hours under argon. After removal of the solvent, the residue was purified by flash chromatography (SiO₂, MeOH-EtOAc 0:1 to 1:9) to afford 1.40 g (31%) of yellow solid, which was characterized spectroscopically. This product was dissolved in CH₂Cl₂ (10 mL) and a solution of HCl in ether (1.0 M, 3.5 mL, 1.6 equiv) was added. After removal of the solvents, the residue was dissolved in CH₂Cl₂ (10 mL) and added dropwise to ether (80 mL) with swirling to give, after filtration, 1.25 g of yellow solid: m.p. 166-167 °C; Anal. Calcd. for C₃₇H₄₂N₄O₅·HCl·0.75 H₂O: C, 66.06; H, 6.67; N, 8.33. Found: C, 66.04; H, 6.57; N, 8.09.

EXAMPLE 54

5-Carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-3-{N-[2-(4,4-diphenylpiperidin-1-yl)ethyl]}carboxamidopyridine hydrochloride hydrate (54). This compound was prepared according to Method A. N-(2-(4,4-

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Diphenylpiperidin-1-yl)ethyl)acetoacetamide (2.34 g, 6.41 mmol, 1.00 equiv), 3-aminocrotonamide (0.706 g, 7.05 mmol, 1.10 equiv) and 4-nitrobenzaldehyde (1.07 g, 7.05 mmol, 1.10 equiv) were stirred together in 2-propanol (40 mL) at reflux for 72 hours under argon. After removal of the solvent, the residue was purified twice by flash chromatography on SiO₂ (1. MeOH-EtOAc 0:1 to 1:5; 2. CH₂Cl₂-NH₃ in MeOH (1.3 M) 12:1) to afford 1.19 g (32%) of yellow solid, which was characterized spectroscopically.

This product (1.05 g, 1.81 mmol, 1.0 equiv) was dissolved in CH₂Cl₂ (10 mL) and a solution of HCl in ether (1.0 M, 2.5 mL, 1.4 equiv) was added. After removal of the solvents, the residue was dissolved in CH₂Cl₂ (10 mL) and added dropwise to ether (80 mL) with swirling to give, after filtration, 0.857 g of yellow solid: m.p. 193-194 °C; Anal. Calcd. for C₂₄H₂₇N₅O₄·HCl·H₂O: C, 64.39; H, 6.36; N, 11.04. Found: C, 64.33; H, 5.98; N, 10.93.

EXAMPLE 55

5-Carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-3-(N-[4-(4,4-diphenylpiperidin-1-yl)butyl])carboxamido-pyridino hydrochloride hydrate (55). This compound was prepared according to Method A. N-(4-(4,4-

Diphenylpiperidin-1-yl)butyl)acetoacetamide (2.86 g, 7.30 mmol, 1.00 equiv), 3-aminocrotonamide (0.804 g, 8.03 mmol, 1.10 equiv) and 4-nitrobenzaldehyde (1.21 g, 8.03 mmol, 1.10 equiv) were stirred together in 2-propanol (50 mL) at reflux for 72 hours under argon. After removal of the solvent, the residue was purified twice by flash chromatography on SiO₂ (1. MeOH-EtOAc 1:4; 2. CHCl₃-NH₃ in MeOH (0.55 M) 85:15) to afford 0.460 g (10%) of yellow solid, which was characterized spectroscopically. This product was dissolved in CH₂Cl₂ (5 mL) and a solution of HCl in ether (1.0 M, 1.0 mL, 1.4 equiv) was added. After removal of the solvents, the residue was dissolved in CH₂Cl₂ (10 mL) and added dropwise to ether (80 mL) with

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swirling to give, after filtration, 0.260 g of yellow solid: m.p. 184-185 °C; Anal. Calcd. for $C_{36}H_{41}N_5O_4 \cdot HCl \cdot H_2O$: C, 65.29; H, 6.70; N, 10.58. Found: C, 65.45; H, 6.40; N, 10.55.

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EXAMPLE 56

1,4-Dihydro-2,6-dimethyl-5-(*N*-methyl)carboxamido-4-(4-nitrophenyl)-3-{*N*-[3-(4-phenylpiperidin-1-yl)propyl]}carboxamidopyridine hydrochloride hemihydrate (56). This compound was prepared according to Method A. *N*-(3-(4-phenylpiperidin-1-yl)propyl)acetoacetamide (1.60 g, 5.30 mmol, 1.00 equiv), *N*-methyl-3-aminocrotonamide (690 mg, 6.10 mmol, 1.15 equiv) and 4-nitrobenzaldehyde (920 mg, 6.10 mmol, 1.15 equiv) were stirred together in 2-propanol (50 mL) at reflux for 78 hours under argon. After removal of the solvent, the residue was purified twice by flash chromatography on SiO_2 (1. MeOH-EtOAc 1:5; 2. $CHCl_3-NH_3$ in MeOH (0.67 M) 100:15). After removal of solvents, the product was dissolved in CH_2Cl_2 (3 mL) and added dropwise into ether (25 mL). The resulting precipitate was filtered and washed with ether (2 x 20 mL) to give 242 mg (8.6%) of yellow solid, which was characterized spectroscopically. This product (205 mg, 0.386 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (3 mL) and a solution of HCl in ether (1.0 M, 0.70 mL, 1.8 equiv) was added. After removal of the solvents, the residue was dissolved in CH_2Cl_2 (3 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 189 mg of yellow solid: m.p. 165-166 °C; Anal. Calcd. for $C_{30}H_{37}N_5O_4 \cdot HCl \cdot 0.5 H_2O$: C, 62.44; H, 6.81; N, 12.14. Found: C, 62.38; H, 6.72; N, 11.86.

EXAMPLE 57

2-(2-Cyanoethyl)-1,2,3,4-tetrahydro-6,7-dimethoxy-isoquinoline. A suspension of 6,7-dimethoxy-1,2,3,4-

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tetrahydroisoquinoline (9.20 g, 40.1 mmol, 1.00 equiv, Aldrich), 3-bromopropionitrile (3.66 mL, 44.1 mmol, 1.10 equiv, Aldrich), potassium carbonate (33.25 g, 240.6 mmol, 6.00 equiv), and potassium iodide (266 mg, 1.60 mmol, 0.04 equiv) in n-butanol (70 mL) and 1,4-dioxane (70 mL) was stirred at reflux under argon for 48 hours. The mixture was cooled to room temperature and concentrated. The residue was purified by flash chromatography (SiO₂, MeOH-EtOAc 0:1 to 1:19) to afford 8.39 g of white solid (59%), which was characterized spectroscopically.

2-(3-Aminopropyl)-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline. To a stirred solution of 2-(2-cyanoethyl)-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (5.70 g, 23.1 mmol, 1.0 equiv) in anhydrous THF (20 mL) under argon was added a solution of BH₃ in THF (1.0 M, 81 mL, 81 mmol, 3.5 equiv) at room temperature. The mixture was stirred at reflux for 4.5 hours and then cooled to room temperature. Aqueous HCl (6 N, 130 mL) was added cautiously at room temperature and stirring was continued for 2.5 hours at 55-60 °C. The mixture was cooled to 0 °C, basified to pH 10-11 by addition of 6 N aq. NaOH, and extracted with CH₂Cl₂ (3 x 100 mL). The combined organic solutions were dried over MgSO₄ and concentrated. To a solution of the residue in CH₂Cl₂ (20 mL) was added HCl in ether (1.0 M, 40 mL, 1.7 equiv). The resulting solution was added dropwise into ether (250 mL) with swirling. The precipitate was filtered and washed with ether (3 x 100 mL). This solid was taken up in water (50 mL), which was basified to pH 10 by addition of 1 M aqueous NaOH, and extracted with CH₂Cl₂ (3 x 100 mL). The combined organic solutions were dried over MgSO₄ and concentrated to give 5.10 g (88%) of white solid, which was characterized spectroscopically.

N-[3-(1,2,3,4-tetrahydro-6,7-dimethoxyisoquinolin-2-

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yl)propyl]acetacetamide. Diketene (1.41 mL, 18.3 mmol, 1.50 equiv) was added at 0 °C to a stirred solution of 2-(3-aminopropyl)-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (3.05 g, 12.2 mmol, 1.00 equiv) in anhydrous THF (30 mL) under argon, and stirring was continued at room temperature for 1.5 hours. The mixture was concentrated and the residual oil washed with hexane (2 x 100 mL) to give 4.07 g (100%) of brown oil, which was characterized spectroscopically and used for the next reaction without purification.

1,4-Dihydro-3-methoxycarbonyl-5-{N-[3-(1,2,3,4-tetrahydro-6,7-dimethoxyisoquinolin-2-yl)propyl]}carboxamide-2,6-dimethyl-4-(4-nitrophenyl)pyridine hydrochloride hydrate (57). This compound was prepared according to Method A. N-[3-(1,2,3,4-tetrahydro-6,7-Dimethoxyisoquinolin-2-yl)propyl]acetoacetamide (2.04 g, 6.09 mmol, 1.00 equiv), methyl 3-aminocrotonate (855 mg, 7.20 mmol, 1.20 equiv) and 4-nitrobenzaldehyde (1.09 g, 7.20 mmol, 1.20 equiv) were stirred together in 2-propanol (50 mL) at reflux for 72 hours under argon. After removal of the solvent, the residue was purified by flash chromatography (SiO₂, MeOH-EtOAc 1:6) to afford 510 mg (15%) of yellow solid, which was characterized spectroscopically. This product was dissolved in CH₂Cl₂ (10 mL) and a solution of HCl in ether (1.0 M, 1.0 mL, 1.1 equiv) was added. After removal of the solvents, the residue was dissolved in CH₂Cl₂ (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 451 mg of yellow solid: m.p. 161-162 °C; Anal. Calcd. for C₂₉H₃₃N₅O₇·HCl·0.75 H₂O: C, 58.63; H, 6.31; N, 9.12. Found: C, 58.79; H, 6.20; N, 8.83.

EXAMPLE 58

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5-Carboxamide-1,4-dihydro-3-{N-[3-(1,2,3,4-tetrahydro-6,7-dimethoxyisoquinolin-2-yl)propyl]}carboxamide-

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2,6-dimethyl-4-(4-nitrophenyl)pyridine hydrochloride (58). This compound was prepared according to Method A. *N*-[3-(1,2,3,4-Tetrahydro-6,7-dimethoxyisoquinolin-2-yl)propyl]acetoacetamide (2.04 g, 6.09 mmol, 1.00 equiv),
5 3-aminocrotonamide (721 mg, 7.20 mmol, 1.20 equiv) and 4-nitrobenzaldehyde (1.09 g, 7.20 mmol, 1.20 equiv) were stirred together in 2-propanol (50 mL) at reflux for 72 hours under argon. After removal of the solvent, the residue was purified twice by flash chromatography on SiO₂
10 (1. CHCl₃-NH₃ in MeOH (0.8 M) 9:1; 2. MeOH-EtOAc 1:6) to afford 400 mg (12%) of yellow solid, which was characterized spectroscopically. This product was dissolved in CH₂Cl₂ (10 mL) and a solution of HCl in ether (1.0 M, 1.0 mL, 1.4 equiv) was added. After removal of
15 the solvents, the residue was dissolved in CH₂Cl₂ (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 310 mg of yellow solid: m.p. 180-181 °C; Anal. Calcd. for C₂₉H₃₅N₅O₆·HCl·0.3 CH₂Cl₂: C, 57.54; H, 6.03; N, 11.45. Found: C, 57.27; H, 5.78; N,
20 11.25.

EXAMPLE 59

N-(3-Bromopropyl)acetoacetamide. Diketene (1.22 mL, 15.7
25 mmol, 1.50 equiv) was added at room temperature to a stirred mixture of 3-bromopropylamine hydrobromide (2.30 g, 10.5 mmol, 1.00 equiv) and triethylamine (1.46 mL, 10.5 mmol, 1.00 equiv) in anhydrous THF (20 mL) under argon, and stirring was continued at room temperature for
30 1 hour. The solvent was removed and the residue was purified by flash chromatography (SiO₂; MeOH-CH₂Cl₂ 0:1 to 1:18) to afford a light yellow oil, 2.10 g (90%), which was characterized spectroscopically.

35 *N*-[3-(1,2,3,4-Tetrahydroisoquinolin-2-yl)propyl]acetoacetamide. A suspension of *N*-(3-bromopropyl)acetoacetamide (4.50 g, 20.3 mmol, 1.00

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equiv), 1,2,3,4-tetrahydroisoquinoline (3.30 mL, 26.3 mmol, 1.30 equiv), K_2CO_3 (3.64 g, 26.3 mmol, 1.30 equiv), and KI (330 mg, 1.99 mmol, 0.10 equiv) in acetone (60 mL) was stirred at reflux for 14 hours. The mixture was cooled to room temperature, filtered, and concentrated. The residue was purified by flash chromatography (SiO_2 , MeOH-EtOAc 0:1 to 1:9) to give 1.78 g (43%) of light yellow oil, which was characterized spectroscopically. *N*-(3-Bromopropyl)acetoacetamide (1.20 g) was also recovered.

1,4-Dihydro-5-{*N*-[3-(1,2,3,4-tetrahydroisoquinolin-2-yl)propyl]}carboxamido-3-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophenyl)pyridine hydrochloride hydrate (59). This compound was prepared according to Method A. *N*-[3-(1,2,3,4-Tetrahydroisoquinolin-2-yl)propyl]acetoacetamide (1.78 g, 6.48 mmol, 1.00 equiv), methyl 3-aminocrotonate (924 mg, 7.77 mmol, 1.20 equiv) and 4-nitrobenzaldehyde (1.18 g, 7.77 mmol, 1.20 equiv) were stirred together in 2-propanol (50 mL) at reflux for 68 hours under argon. After removal of the solvent, the residue was purified by flash chromatography (SiO_2 , MeOH-EtOAc 1:9) to afford 824 mg (25%) of yellow solid, which was characterized spectroscopically. This product was dissolved in CH_2Cl_2 (10 mL) and a solution of HCl in ether (1.0 M, 2.3 mL, 1.4 equiv) was added. After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 690 mg of yellow solid: m.p. 145-146 °C; Anal. Calcd. for $C_{28}H_{32}N_4O_5 \cdot HCl \cdot 0.25 H_2O$: C, 61.65; H, 6.19; N, 10.27. Found: C, 61.82; H, 6.15; N, 10.15.

EXAMPLE 60

5-Carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-3-{*N*-[3-(4-phenylpiperidin-1-yl)propyl]}carboxamido-pyridine (60). This compound was prepared according to

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Method B. The suspension of 5-carboxamido-1,4-dihydro-2,6-dimethyl-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (90 mg, 0.28 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (59 mg, 0.31 mmol) in 15 mL of CH_2Cl_2 was stirred at 0°C for 20 min. To this suspension was added the solution of 3-(4-phenylpiperidin-1-yl)propylamine (68 mg, 0.473 mmol) in 2 mL of CH_2Cl_2 . The mixture was stirred at r.t. for 3 days. The mixture was washed with water (2×10 mL) followed by saturated brine (10 mL). After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was charged to SiO_2 prep-TLC and eluted with $\text{CHCl}_3/\text{MeOH}/\text{NH}_3$ (2N in MeOH) mixture (ratio=90:8:4). The desired product was collected and precipitated from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to afford 27 mg (18% yield) of yellowish powder: M.p. $100-105^\circ\text{C}$; Calcd for $\text{C}_{27}\text{H}_{33}\text{N}_5\text{O}_5 \cdot 3/4\text{H}_2\text{O}$: C 65.58, H 6.93, N 13.19; Found: C 65.94, H 6.53, N 12.81.

EXAMPLE 61

5-Carboxamido-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamide-pyridine (61). This compound was prepared according to Method B. 5-Carboxamido-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine was prepared by refluxing the solution of 3-aminocrotonamide (3.696 g, 36.9 mmol), 3-nitrobenzaldehyde (5.576 g, 36.9 mmol) and 2-cyanoethyl acetoacetate (2.864 g, 18.5 mmol) in 100 mL of EtOH for 48 hrs. After work up, the reaction mixture was purified by chromatography (SiO_2 , MeOH: CHCl_3 , 10:90) to give a yellow oil (4.762 g, 69.5% yield). The cyanoethyl ester (2.90 g, 7.83 mmol) thus prepared was hydrolyzed by 2N KOH and 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3-carboxylic acid (1.632 g, 65.7% yield) was obtained as a bright yellow powder.

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A suspension of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3-carboxylic acid (136 mg, 0.429 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (82 mg, 0.429 mmol) and 3-(4,4-diphenylpiperidin-1-yl)propylamine (126 mg, 0.429 mmol) in 15 mL of CH_2Cl_2 was stirred at refluxing conditions overnight. The mixture was washed with water (2 x 10 mL) and brine (10 mL). After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was charged to SiO_2 prep-TLC and eluted with $\text{CHCl}_3/\text{MeOH}/\text{NH}_3$ (2N in MeOH) mixture (ratio=90:8:4). The desired product was collected and precipitated from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to afford 59 mg (23% yield) of yellowish powder: M.p. 144-148 °C; Calcd for $\text{C}_{33}\text{H}_{39}\text{N}_5\text{O}_4 \cdot 3/4\text{H}_2\text{O}$: C 69.23, H 6.72, N 11.52; Found: C 69.16, H 6.25, N 11.32.

EXAMPLE 62

5-Carboxamido-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3-{N-[3-(4-phenylpiperidin-1-yl)propyl]}carboxamide-pyridine (62). This compound was prepared according to Method B. The suspension of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)pyridine-3-carboxylic acid (136 mg, 0.429 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (82 mg, 0.429 mmol) and 3-(4-phenylpiperidin-1-yl)propylamine (94 mg, 0.429 mmol) in 15 mL of CH_2Cl_2 was stirred at refluxing conditions overnight. The mixture was washed with water (2 x 10 mL) and brine (10 mL). After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was charged to SiO_2 prep-TLC and eluted with $\text{CHCl}_3/\text{MeOH}/\text{NH}_3$ (2N in MeOH) mixture (ratio=90:8:4). The desired product was collected and precipitated from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to afford 75 mg (33% yield) of yellowish powder: M.p. 92-96 °C; Calcd for $\text{C}_{27}\text{H}_{33}\text{N}_5\text{O}_4 \cdot 3/4\text{H}_2\text{O}$: C 65.58, H 6.93, N 13.19; Found: C 65.96, H 6.54, N 13.04.

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EXAMPLE 63

1,4-Dihydro-6-methyl-4-(4-nitrophenyl)-5-{N-[3-(4-
phenylpiperidin-1-yl)propyl]}carboxamide-[2,3,d]uracilyl-
5 pyridino (63). This compound was prepared according to
Method B. 5-(2-Cyanoethoxy)carbonyl-1,4-dihydro-6-
methyl-4-(4-nitrophenyl)-[2,3,d]uracilylpyridine was
prepared by refluxing the solution of 4-amino-2,6-
dihydroxypyrimidine (820 mg, 6.40 mmol), 4-
10 nitrobenzaldehyde (973 mg, 6.40 mmol) and 2-cyanoethyl
acetoacetate (1.00 g, 6.40 mmol) in 100 mL of 2-propanol
for 72 hrs. The product, a white precipitate, was
collected by filtration, washed with 10 mL of cold 2-
propanol, 10 mL of cold MeOH, then dried in vacuo to give
15 1.19 g (46.8% yield) of white powder. The cyanoethyl
ester (500 mg, 1.26 mmol) thus prepared was hydrolyzed by
2N KOH and 1,4-dihydro-6-methyl-4-(4-nitrophenyl)-
[2,3,d]uracilylpyridine-5-carboxylic acid (255 mg, 58.8%
yield) was obtained as a yellowish powder.

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A suspension of 1,4-dihydro-6-methyl-4-(4-
nitrophenyl)-[2,3,d]uracilylpyridine-5-carboxylic acid
(100 mg, 0.30 mmol), 1-(3-dimethylaminopropyl)-3-
ethylcarbodiimide hydrochloride (58 mg, 0.30 mmol) and 3-
25 (4-phenylpiperidin-1-yl)propylamine (66 mg, 0.30 mmol) in
40 mL of CH_2Cl_2 was stirred at r.t. for 48 hrs. The
mixture was washed with water (2 x 10 mL), followed by
washed with 10% NaHCO_3 (10 mL). After drying with MgSO_4
and removal of solvent, a yellowish oil was obtained,
30 which was purified by chromatography (SiO_2 , MeOH: CHCl_3 ,
10:90). The product was precipitated from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to
afford 21 mg (13% yield) of yellowish powder: M.p. 202-
205 °C; Calcd for $\text{C}_{27}\text{H}_{32}\text{N}_6\text{O}_5$: C 63.95, H 5.92, N 15.43;
Found: C 63.71, H 5.71, N 15.30.

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EXAMPLE 64

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1,4-Dihydro-6-methyl-4-(4-nitrophenyl)-5-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamide-[2,3,d]uracilylpyridine (64). This compound was prepared according to Method B. The suspension of 1,4-dihydro-6-methyl-4-(4-nitrophenyl)-[2,3,d]uracilylpyridine-5-carboxylic acid (100 mg, 0.30 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (58 mg, 0.30 mmol) and 3-(4,4-diphenylpiperidin-1-yl)propylamine (86 mg, 0.30 mmol) in 50 mL of CH_2Cl_2 was stirred at r.t. for 48 hrs. The mixture was washed with water (2 x 10 mL) and 10% NaHCO_3 (10 mL). After drying with MgSO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3$, 10:90). The product was precipitated from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ to afford 25 mg (13% yield) of yellowish powder: M.p. 184-186 °C; Calcd for $\text{C}_{35}\text{H}_{34}\text{N}_6\text{O}_5\cdot\text{CO}_2$: C 65.05, H 5.46, N 12.64; Found: C 65.43, H 5.69, N 12.21.

EXAMPLE 65

2-(furan-3-yl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-5-{N-[3-(4-phenylpiperidin-1-yl)propyl]}carboxamidopyridine hydrochloride hydrate (64). This compound was prepared according Method B from 86.8 mg of 2-(furan-3-yl)-1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine (0.200 mmol) and 65.5 mg of 1-(3-aminopropyl)-4-phenylpiperidine (0.300 mmol) in 3 mL of dry THF. The crude product was chromatographed on 100 g of silica (gradient elution: 5% to 20% $\text{MeOH}-\text{EtOAc}$) to give 110 mg of 2-(furan-3-yl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-5-{N-[3-(4-phenylpiperidin-1-yl)propyl]}carboxamidopyridine as a yellow foamy solid (94%). The free base (98 mg) was dissolved in 0.5 mL of dichloromethane and added to 1 mL of 1 M HCl in ether. The precipitate was collected, washed with 5 mL of ether, and dried to give a yellow

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powder: mp 205-210 °C (decomp.); Anal. Calcd for $C_{33}H_{36}N_4O_6 \cdot HCl \cdot 1.2 H_2O$: C, 61.67; H, 6.18; N, 8.72. Found: C, 61.53; H, 5.71; N, 9.01.

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EXAMPLE 66

5-Carboxamido-2-(furan-3-yl)-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-{N-[N-phenylmethyl)piperidin-4-yl]}carboxamidopyridine hydrochloride hydrate (66). This compound was prepared according to Method B from 50.0 mg of 5-carboxamido-2-(furan-3-yl)-1,4-dihydro-3-(imidazol-1-yl)carbonyl-6-methyl-4-(4-nitro)phenylpyridine (0.115 mmol) and 32.9 mg of N-benzyl-4-aminopiperidine (0.173 mmol) in 3 mL of dry THF. The crude product was chromatographed on 100 g of silica (EtOAc) to give 56 mg of the free base (87%) as a yellow foamy solid. The free base (45 mg) was dissolved in 2 mL of dichloromethane and added to 3 mL of 0.33 M HCl in ether. The precipitate was collected, washed with 5 mL of ether, and dried to give a yellow powder: mp 210-215 °C (decomp.); Anal. Calcd for $C_{31}H_{32}N_4O_6 \cdot HCl \cdot H_2O$: C, 60.93; H, 5.77; N, 9.17. Found: C, 60.93; H, 5.35; N, 9.07.

EXAMPLE 67

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5-Carboxamido-2-(furan-3-yl)-1,4-dihydro-6-methyl-3-{N-[3-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl)propyl]}carboxamido-4-(4-nitro)phenylpyridine hydrochloride hydrate (67). This compound was prepared according to Method B from 51.1 mg of 5-carboxamido-2-(furan-3-yl)-1,4-dihydro-3-(imidazol-1-yl)carbonyl-6-methyl-4-(4-nitro)phenylpyridine (0.118 mmol) and 38.3 mg of 2-(3-aminopropyl)-1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline (0.153 mmol) in 3 mL of dry THF. The crude product was chromatographed on 100 g of silica (gradient elution: 5% to 15% MeOH-EtOAc) to give the free base as a yellow foamy solid (71%). The free base (50

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mg) was dissolved in 2 mL of dichloromethane and added to 3 mL of 0.33 M HCl in ether. The precipitate was collected, washed with 5 mL of ether, and dried to give a yellow powder: mp 211-221 °C (decomp.);

- 5 Anal. Calcd for $C_{33}H_{36}N_4O_8 \cdot HCl \cdot 0.5H_2O$: C, 59.86; H, 5.78; N, 8.46. Found: C, 59.96; H, 5.57; N, 8.45.

EXAMPLE 68

- 10 **2-Cyanoethyl 3-Oxohexanoate.** A mixture of ethyl 3-oxohexanoate (33.7 mmol) and 3-hydroxypropionitrile (28.1 mmol) were placed in a round bottom flask (magnetically stirred) equipped with a short distillation path. The resulting mixture was gradually heated to 180-205 °C in an
15 oil bath. The distillate was collected. The mixture was then cooled to room temperature and the residue was distilled under reduced pressure to give 2-cyanoethyl 3-oxohexanoate.
- 20 **1,4-Dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-2-propylpyridine-3-carboxylic Acid.** A mixture of 2-cyanoethyl 3-oxohexanoate (11.9 mmol), methyl 3-aminocrotonate (11.9 mmol), and 4-nitrobenzaldehyde in 25 mL of isopropanol were heated at reflux temperature for
25 16 h, cooled, and the solvent was removed under reduced pressure. The residue was dissolved in 15 mL of dioxane (slightly warmed with a heat gun to dissolve the product) and 626 mg of NaOH in 15 mL of water was added to the reaction mixture. After 0.5 hrs, the maroon solution was
30 concentrated to a small volume under reduced pressure, partitioned between 50 mL of water and 50 mL of ethyl acetate, separated, and the aqueous solution was washed with 2 X 20 mL of ethyl acetate. The aqueous extract was acidified with concentrated HCl (pH = 2), and the
35 precipitated oil was extracted with ethyl acetate (2 X 40 mL). The combined organic extracts were dried ($MgSO_4$), and the solvent was removed in vacuo to give the desired

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product as a foamy yellow solid. The acid was used in the next step without further purification.

3-(Imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-propylpyridine. A solution of 1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-propylpyridine-3-carboxylic acid (2.89 mmol) and carbonyldiimidazole (3.75 mmol) in 20 mL of anhydrous THF are stirred at room temperature for 12 hours; solvent was removed in vacuo, and the crude product was chromatographed on silica. The column was eluted with MeOH-EtOAc to give the title compound as a yellow oily solid.

1,4-Dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carbamate)-2-propylpyridine (68). A solution of 3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-propylpyridine (0.456 mmol) and 1-(3-aminopropyl)-4,4-diphenylpiperidine (1.06 mmol) in 5 mL of dry THF are heated at reflux temperature for 19 hrs, cooled to room temperature. The solvent was removed in vacuo and the crude product is chromatographed on 50 g of silica packed with 5% MeOH-EtOAc. The column was eluted with MeOH-EtOAc to afford the title compound as a yellow foamy solid. To this product was added HCl in ether (1 M) in a minimum amount of ethyl acetate. The precipitate was collected, washed with ether (2 X 5 mL), and dried to give the hydrochloride salt as a yellow powder, which was characterized spectroscopically. The fumarate salt was prepared by mixing fumaric acid (8.7 mg, 0.0749 mmol) and the free base (0.0749 mmol) in 2 mL of 1:1 acetone-water. The product was purified by recrystallization.

EXAMPLE 69

2,2-Dimethyl-5-(1-octenyl)-1,3-dioxane-4,6-dione. Carbonyldiimidazole (71.7 g, 0.442 mol) was added

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portionwise to a stirred solution of heptanoic acid (0.402 mol) in 300 mL of dry dichloromethane. The resulting mixture was stirred at room temperature for 2 hours. A solution of pyridine (35.8 mL, 0.442 mol) and
5 Meldrum's acid (63.7 g, 0.442 mol) in 150 mL of dry dichloromethane were added over a period of 2 hours to the reaction mixture. The reaction mixture was stirred for 16 hours, quenched with 400 mL of 2 N HCl (bubbling), separated, washed sequentially with 2 x 400 mL 2 N HCl,
10 brine (400 mL), dried (MgSO₄), and the solvent was removed in vacuo to give the title compound as a viscous oil. The crude product was used in the next step after spectral characterization.

15 2-Cyanoethyl 3-Oxoheptanoate: A mixture of 2,2-dimethyl-5-(1-oxoheptyl)-1,3-dioxane-4,6-dione (29.4 mmol) and 3-hydroxypropionitrile (4.48 g, 63.0 mmol) in 25 mL of dry toluene were heated at reflux temperature for 1 hour. The solvent was removed in vacuo, and the residue was
20 chromatographed on silica gel to give the title compound as a viscous oil, which was used in the next step after spectral characterization.

2-Methyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridino-3-carboxylic acid. A mixture of 2-cyanoethyl 3-oxooctanoate (11.9 mmol), methyl 3-aminocrotonate (11.9 mmol), and 4-nitrobenzaldehyde in 25 mL of isopropanol are heated at reflux temperature for 16 h, cooled, and the solvent is removed under reduced
30 pressure. The residue is dissolved in 15 mL of dioxane and 626 mg of NaOH in 15 mL of water is added to the reaction mixture. After 0.5 hr, the solution is concentrated to a small volume under reduced pressure, partitioned between 50 mL of water and 50 mL of ethyl
35 acetate, separated, and the aqueous solution is washed with 2 x 20 mL of ethyl acetate. The organic solutions are discarded. The aqueous extract is acidified with

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concentrated HCl (pH = 2), and the precipitated oil is extracted with ethyl acetate (2 X 40 mL). The combined organic extracts are dried (MgSO₄), and the solvent is removed in vacuo to give a residue, which is
5 characterized spectroscopically.

2-Moxyl-1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine. A solution of 2-hexyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (2.89
10 mmol) and carbonyldiimidazole (3.75 mmol) in 20 mL of anhydrous THF is stirred at room temperature for 12 hrs. The solvent is removed in vacuo, and the crude product is chromatographed on silica and characterized
15 spectroscopically.

2-Moxyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-3-(N-(4,4-diphenylpiperidin-1-yl)propyl)carbamidopyridine (69). This compound is prepared
20 according to Method B. A solution of 2-hexyl-1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine (0.456 mmol) and 1-(3-aminopropyl)-4,4-diphenylpiperidine (1.06 mmol) in 5 mL of dry THF are heated at reflux temperature for 19 hrs
25 and then cooled to room temperature. The solvent is removed in vacuo. The crude product is purified by flash chromatography and characterized spectroscopically. The hydrochloride salt is prepared by addition of HCl in ether (1 M) to the free base in a minimum amount of ethyl acetate. The precipitate is collected, washed with ether
30 (2 X 5 mL), dried, and purified by recrystallization. The fumarate salt is prepared by mixing fumaric acid (8.7 mg, 0.0749 mmol) and the free base (0.0749 mmol) in 2 mL of 1:1 acetone-water. The product is purified by
35 recrystallization.

EXAMPLE 70

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1,4-Dihydro-4-(4-methoxyphenyl)-5-methoxycarbonyl-6-methyl-2-propylpyridine-3-carboxylic acid. A mixture of 2-cyanoethyl 3-oxohexanoate (11.9 mmol), methyl 3-aminocrotonate (11.9 mmol), and 4-methoxybenzaldehyde in 25 mL of isopropanol is heated at reflux temperature for 16 h, cooled, and the solvent is removed under reduced pressure. The residue is dissolved in 15 mL of dioxane and 626 mg of NaOH in 15 mL of water is added to the reaction mixture. After 0.5 hrs, the solution is concentrated to a small volume under reduced pressure, partitioned between 50 mL of water and 50 mL of ethyl acetate, separated, and the aqueous solution is washed with 2 X 20 mL of ethyl acetate. The organic solutions are discarded. The aqueous extract is acidified with concentrated HCl (pH = 2), and the precipitated oil is extracted with ethyl acetate (2 X 40 mL). The combined organic extracts are dried (MgSO₄), and the solvent is removed in vacuo to give a residue, which is characterized spectroscopically.

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2-Methyl-1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-4-(4-methoxy)phenyl-6-methylpyridine. A solution of 1,4-dihydro-4-(4-methoxyphenyl)-5-methoxycarbonyl-6-methyl-2-propylpyridine-3-carboxylic acid (2.89 mmol) and carbonyldiimidazole (3.75 mmol) in 20 mL of anhydrous THF are stirred at room temperature for 12 hrs. The solvent is removed in vacuo. The product is purified by flash chromatography and characterized spectroscopically.

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1,4-Dihydro-5-methoxycarbonyl-6-methyl-4-(4-methoxy)phenyl-3-(N-(4,4-diphenylpiperidine-1-yl)propyl)carbamido-2-propylpyridine (70). This compound is prepared according to Method B. A solution of 1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-4-(4-methoxy)phenyl-6-methyl-2-propylpyridine (0.456 mmol) and 1-(3-aminopropyl)-4,4-diphenylpiperidine (1.06 mmol) in

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5 mL of dry THF is heated at reflux temperature for 19 hrs. The solvent is removed in vacuo. The crude product is purified by flash chromatography and characterized spectroscopically. The hydrochloride salt is prepared by addition of HCl in ether (1 M) to the free base in a minimum amount of ethyl acetate. The precipitate is collected, washed with ether (2 X 5 mL), dried, and purified by recrystallization. The fumarate salt is prepared by mixing fumaric acid (8.7 mg, 0.0749 mmol) and the free base (0.0749 mmol) in 2 mL of 1:1 acetone-water. The product is purified by recrystallization.

EXAMPLE 71

15 4-(4-Chlorophenyl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-2-propylpyridino-3-carboxylic acid. A mixture of 2-cyanoethyl 3-oxohexanoate (11.9 mmol), methyl 3-aminocrotonate (11.9 mmol), and 4-chlorobenzaldehyde in 25 mL of isopropanol is heated at reflux temperature for 16 h, cooled, and the solvent is removed under reduced pressure. The residue is dissolved in 15 mL of dioxane and 626 mg of NaOH in 15 mL of water is added to the reaction mixture. After 0.5 hrs, the solution is concentrated to a small volume under reduced pressure, partitioned between 50 mL of water and 50 mL of ethyl acetate, separated, and the aqueous solution is washed with 2 X 20 mL of ethyl acetate. The organic solutions are discarded. The aqueous extract is acidified with concentrated HCl (pH = 2), and the precipitated oil is extracted with ethyl acetate (2 X 40 mL). The combined organic extracts are dried (MgSO₄), and the solvent is removed in vacuo to give a residue, which is characterized spectroscopically.

35 4-(4-Chlorophenyl)-1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-2-propylpyridino. A solution of 4-(4-chlorophenyl)-1,4-dihydro-5-methoxycarbonyl-6-

methyl-2-propylpyridine-3-carboxylic acid (2.89 mmol) and carbonyldiimidazole (3.75 mmol) in 20 mL of anhydrous THF is stirred at room temperature for 12 hrs. The solvent is removed in vacuo. The product is purified by flash chromatography and characterized spectroscopically.

4-(4-Chlorophenyl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-3-(N-(4,4-diphenylpiperidin-1-yl)propyl)carbamate-2-propylpyridine (71). This compound is prepared according to Method B. A solution of 4-(4-chlorophenyl)-1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-2-propylpyridine (0.456 mmol) and 1-(3-aminopropyl)-4,4-diphenylpiperidine (1.06 mmol) in 5 mL of dry THF is heated at reflux temperature for 19 hrs. The solvent is removed in vacuo. The crude product is purified by flash chromatography and characterized spectroscopically. The hydrochloride salt is prepared by addition of HCl in ether (1 M) to the free base in a minimum amount of ethyl acetate. The precipitate is collected, washed with ether (2 X 5 mL), dried, and purified by recrystallization. The fumarate salt is prepared by mixing fumaric acid (8.7 mg, 0.0749 mmol) and the free base (0.0749 mmol) in 2 mL of 1:1 acetone-water. The product is purified by recrystallization.

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EXAMPLE 72

1,4-Dihydro-5-methoxycarbonyl-6-methyl-4-(4-methylphenyl)phenyl-2-propylpyridine-3-carboxylic acid. A mixture of 2-cyanoethyl 3-oxohexanoate (11.9 mmol), methyl 3-aminocrotonate (11.9 mmol), and 4-methylbenzaldehyde in 25 mL of isopropanol are heated at reflux temperature for 16 h, cooled, and the solvent is removed under reduced pressure. The residue is dissolved in 15 mL of dioxane and 626 mg of NaOH in 15 mL of water is added to the reaction mixture. After 0.5 hrs, the solution is concentrated to a small volume under reduced

pressure, partitioned between 50 mL of water and 50 mL of ethyl acetate, separated, and the aqueous solution is washed with 2 X 20 mL of ethyl acetate. The organic solutions are discarded. The aqueous extract is acidified with concentrated HCl (pH = 2), and the precipitated oil is extracted with ethyl acetate (2 X 40 mL). The combined organic extracts are dried (MgSO₄), and the solvent is removed in vacuo to give a residue, which is characterized spectroscopically.

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1,4-Dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-methylphenyl)-2-propylpyridine. A solution of 1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-methylphenyl)-2-propylpyridine-3-carboxylic acid (2.89 mmol) and carbonyldiimidazole (3.75 mmol) in 20 mL of anhydrous THF is stirred at room temperature for 12 hrs. The solvent is removed in vacuo. The product is purified by flash chromatography and characterized spectroscopically.

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1,4-Dihydro-5-methoxycarbonyl-6-methyl-4-(4-methylphenyl)-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carbamide)-2-propylpyridine (72). This compound is prepared according to Method B. A solution of 1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-methylphenyl)-2-propylpyridine (0.456 mmol) and 1-(3-aminopropyl)-4,4-diphenylpiperidine (1.06 mmol) in 5 mL of dry THF is heated at reflux temperature for 19 hrs. The solvent is removed in vacuo. The crude product is purified by flash chromatography and characterized spectroscopically. The hydrochloride salt is prepared by addition of HCl in ether (1 M) to the free base in a minimum amount of ethyl acetate. The precipitate is collected, washed with ether (2 X 5 mL), dried, and purified by recrystallization. The fumarate salt is prepared by mixing fumaric acid (8.7 mg, 0.0749 mmol) and the free base (0.0749 mmol) in 2 mL

of 1:1 acetone-water. The product is purified by recrystallization.

EXAMPLE 73

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2-Ethyl-1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine. A solution of 1.00 g of 2-ethyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-methylphenyl)pyridine-3-carboxylic acid (2.89 mmol) and 609 mg of carbonyldiimidazole (3.75 mmol) in 20 mL of anhydrous THF were stirred at room temperature for 12 hrs. The solvent was removed in vacuo, and the crude product was chromatographed on 200 g of silica packed with 1% MeOH-EtOAc. The column was eluted with 1% (0.5 L), 2%, (0.5 L), and 3% (1 L) MeOH-EtOAc to give 350 mg (31%) of yellow oily solid, which was characterized spectroscopically.

20 2-Ethyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (73). This compound was prepared according to Method B. A solution of 181 mg of 2-ethyl-1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine (0.456 mmol) and 300 mg of 1-(3-aminopropyl)-4,4-diphenylpiperidine (1.06 mmol) in 5 mL of dry THF was heated at reflux temperature for 19 hrs and then cooled to room temperature. The solvent was removed in vacuo and the crude product was chromatographed on 50 g of silica packed with 5% MeOH-EtOAc. The column was eluted with 0.5 L of 10% and 0.5 L of 15% MeOH-EtOAc to afford 270 mg (95%) of yellow foamy solid, which was characterized spectroscopically. To a solution of this free base (124 mg) in EtOAc (0.5 mL) was added HCl in ether (1 mL, 1 M). The precipitate was collected, washed with ether (2 X 5 mL), and dried to give a yellow powder:

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mp 240-245 °C (decomp.); Anal. Calcd for $C_{37}H_{42}N_4O_5 \cdot HCl \cdot H_2O$: C, 65.62; H, 6.70; N, 8.27. Found: C, 65.57; H, 6.49; N, 8.31.

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EXAMPLE 74

2-Ethyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4-phenylpiperidin-1-yl)propyl))carbamidopyridino hydrochloride hydrate (74). This compound was prepared according to Method B from 97.4 mg of 2-ethyl-1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine (0.246 mmol) and 80.7 mg of 1-(3-aminopropyl)-4-phenylpiperidine (0.369 mmol) in 3 mL of dry THF. The crude product was chromatographed on 100 g of silica (gradient elution: 5% to 25% MeOH-EtOAc) to give 128 mg (95%) of foamy yellow solid. This free base (45 mg) was dissolved in 2 mL of dichloromethane and added to 3 mL of 0.33 M HCl in ether. The precipitate was collected, washed with 5 mL of ether, and dried to give a yellow powder: mp 209-214 °C (decomp.); Anal. Calcd for $C_{37}H_{42}N_4O_5 \cdot HCl \cdot H_2O$: C, 61.94; H, 6.87; N, 9.32. Found: C, 62.14; H, 6.37; N, 9.39.

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EXAMPLE 75

2-Ethyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-3-(N-(N-phenylmethyl)piperidin-4-yl)carbamidopyridino hydrochloride (75). This compound was prepared according to Method B from 63.1 mg of 2-ethyl-1,4-dihydro-3-(imidazol-1-yl)carbonyl-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine (0.159 mmol) and 45.4 mg of N-benzyl-4-aminopiperidine (0.239 mmol) in 3 mL of dry THF. The crude product was chromatographed on 100 g of silica (gradient elution: 1% to 2% MeOH-EtOAc) to give 56 mg (87%) of foamy yellow solid (87%). This free base (50 mg) was dissolved in 0.5

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mL of dichloromethane and added to 3 mL of 0.33 M HCl in ether. The precipitate was collected, washed with 5 mL of ether, and dried to give a yellow powder: mp 221-224 °C (decomp.); Anal. Calcd for $C_{29}H_{34}N_4O_7 \cdot HCl$: C, 62.75; H, 6.36; N, 10.09. Found: C, 62.47; H, 6.06; N, 9.94.

EXAMPLE 76

5-Carboxamide-2-ethyl-1,4-dihydro-3-(N-(3-(1,2,3,4-tetrahydro-6,7-dinotherynequinolin-2-yl)propyl))carboxamide-6-methyl-4-(4-nitro)phenylpyridine hydrochloride hydrate (76). This compound was prepared according to Method B from 64.3 mg of 5-carboxamido-2-ethyl-1,4-dihydro-3-(imidazol-1-yl)carbonyl-6-methyl-4-(4-nitro)phenylpyridine (0.162 mmol) and 69.9 mg of 2-(3-aminopropyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisquinoline (0.243 mmol) in 3 mL of dry THF. The crude product was chromatographed on 100 g of silica (gradient elution: 5% to 15% MeOH-EtOAc) to give 67 mg (71%) of foamy yellow solid. This free base (50 mg) was dissolved in 0.5 mL of dichloromethane and added to 3 mL of 0.33 M HCl in ether. The precipitate was collected, washed with 5 mL of ether, and dried to give a yellow powder: mp 200-204 °C (decomp.); Anal. Calcd for $C_{31}H_{35}N_5O_7 \cdot HCl \cdot 0.5H_2O$: C, 59.15; H, 6.50; N, 8.90. Found: C, 59.27; H, 5.89; N, 9.10.

EXAMPLE 77

5-Carboxamide-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(4-(4-phenylpiperidin-1-yl)butyl))carboxamidopyridine hydrochloride hydrate (77). This compound was prepared according to Method B from 102 mg of 5-carboxamido-2-ethyl-1,4-dihydro-3-(imidazol-1-yl)carbonyl-6-methyl-4-(4-nitro)phenylpyridine (0.258 mmol) and 90.0 mg of 1-(4-aminobutyl)-4-phenylpiperidine (0.387 mmol) in 3 mL of dry THF. The crude product was chromatographed on 100 g of silica (gradient elution: 10%

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to 20% MeOH-EtOAc) to give 131 mg (91%) of foamy yellow solid. This free base (40 mg) was dissolved in 0.5 mL of dichloromethane and added to 3 mL of 0.33 M HCl in ether. The precipitate was collected, washed with 5 mL of ether, and dried to give a yellow powder: mp 190-195 °C (decomp.); Anal. Calcd for $C_{12}H_{10}N_2O_5 \cdot HCl \cdot H_2O$: C, 62.48; H, 7.05; N, 9.11. Found: C, 62.87; H, 6.87; N, 9.15.

EXAMPLE 78

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1,4-Dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-2-phenylpyridine-3-carboxylic acid. A solution of 5.01 g of 2-cyanoethyl 3-phenyl-3-oxopropionate (23.1 mmol), 6.98 g of 4-nitrobenzaldehyde (46.2 mmol), and 5.32 g of methyl 3-aminocrotonate (46.2 mmol) in 100 mL of isopropanol were heated at reflux temperature for 2 days, cooled, and the solvent was removed in vacuo. The residue was dissolved in 50 mL of warm dioxane and 1.21 g of NaOH in 25 mL of water was added to the reaction mixture. The resulting maroon solution was stirred for 3 hrs. The solvent was removed in vacuo. The residue was partitioned between water (100 mL) and ethyl acetate (50 mL), separated, and washed with ethyl acetate (3 X 50 mL). The aqueous extract was acidified with concentrated HCl (pH 2-3), the precipitated solids were filtered, and washed with water (2 X 20 mL). The crude product was recrystallized from acetone-water mixture to give 5.02 g (55%) of yellow amorphous solid: mp 190-191 °C; Anal. Calcd for $C_{21}H_{15}N_2O_5$: C, 63.96; H, 4.60; N, 7.10. Found: C, 63.86; H, 4.59; N, 7.04.

1,4-Dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carbamidopyridine hydrochloride hydrate (78). This compound was prepared according to Method B. A mixture of 394 mg of 1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-phenylpyridine-3-carboxylic

acid (1.00 mmol), 310 mg of DCC (1.50 mmol), and 134 mg of DMAP (1.10 mmol) in 10 mL of dry dichloromethane were stirred at room temperature for 1h. 1-(3-Aminopropyl)-4,4-diphenylpiperidine (339 mg, 1.20 mmol) was added and the mixture was heated at reflux temperature for 2 hrs. The reaction mixture was cooled, filtered, and chromatographed on 200 g of silica packed with 10% MeOH-EtOAc. The column was eluted with 10% (0.5 L), 15% (1 L), and 20% (0.5 L) MeOH-EtOAc to give 628 mg (95%) of yellow foamy solid. This free base (317 mg) was dissolved in 5 mL of dichloromethane and added to 15 mL of 0.33 M HCl in ether. The precipitate was collected, washed with 5 mL of ether, and dried to give a yellow powder: mp 210-215 °C (decomp.); Anal. Calcd for $C_{41}H_{42}N_4O_5 \cdot HCl$: C, 69.63; H, 6.13; N, 7.92. Found: C, 69.33; H, 6.34; N, 7.86.

EXAMPLE 79

1,4-Dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-phenyl-3-(N-(3-(4-phenylpiperidin-1-yl)propyl))carboxamidopyridine hydrochloride (79). This compound was prepared according to Method B from 205 mg of 1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-phenylpyridine-3-carboxylic acid (0.520 mmol), 161 mg of DCC (0.780 mmol), 70 mg of DMAP (0.572 mmol), and 121 mg of 1-(4-aminobutyl)-4-phenylpiperidine (0.520 mmol) in 10 mL of dry dichloromethane. The crude product was chromatographed on 100 g of silica (gradient elution: 5% to 15% MeOH-EtOAc) to give 290 mg (96%) of foamy yellow solid. This free base (280 mg) was dissolved in 5 mL of dichloromethane and added to 15 mL of 0.33 M HCl in ether. The precipitate was collected, washed with 2 X 5 mL of ether, and dried to give a yellow powder: mp 196-201 °C (decomp.); Anal. Calcd for $C_{36}H_{40}N_4O_5 \cdot HCl \cdot 0.5H_2O$: C, 66.10; H, 6.47; N, 8.56. Found: C, 66.07; H, 6.09; N, 8.46.

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EXAMPLE 80

5-Carboxamide-1,4-dihydro-4-(4-nitro)phenyl-2-phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carbox-
5 amidepyridino hydrochloride (80). This compound was prepared according to Method B from 99.0 mg of 5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-2-phenylpyridine-3-carboxylic acid (0.261 mmol), 80.8 mg of DCC (0.391 mmol), 35.1 mg of DMAP (0.287 mmol), and 88.4
10 mg of 1-(3-aminopropyl)-4,4-diphenylpiperidine (0.313 mmol) in 5 mL of dry dichloromethane (24 hrs of reflux). The crude product was chromatographed on 200 g of silica (gradient elution: 20% to 25% MeOH-EtOAc) to give 20 mg (18%) of foamy yellow solid. This free base was
15 dissolved in 1 mL of dichloromethane and added to 2 mL of 0.5 M HCl in ether. The precipitate was collected, washed with 5 mL of ether, and dried to give a yellow powder: mp 225-230 °C (decomp.); Anal. Calcd for $C_{28}H_{26}N_4O_5 \cdot HCl \cdot 0.8 CH_2Cl_2$: C, 64.46; H, 5.78; N, 9.21. Found:
20 C, 64.42; H, 5.76; N, 9.19.

EXAMPLE 81

5-Carboxamide-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidepyridino hydrochloride (81). This compound was prepared according to Method B from 550 mg of 5-carboxamido-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (88% pure by
25 spectral analyses) (1.46 mmol), 514 mg of DCC (2.49 mmol), 223 mg of DMAP (1.83 mmol), and 523 mg of 1-(3-aminopropyl)-4,4-diphenylpiperidine (1.99 mmol) in 20 mL of dry dichloromethane (12 hrs of reflux). The crude product was chromatographed on 200 g of silica (gradient
30 elution: 1:1:50 to 2:2:50 MeOH-isopropyl amine-EtOAc) to give 720 mg (74%) of foamy yellow solid (contains one equivalent of EtOAc). This free base (350 mg) was
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dissolved in 5 mL of dichloromethane and added to 20 mL of 0.25 M HCl in ether. The precipitate was collected, washed with 3 X 5 mL of ether, and dried to give a yellow powder: mp 243-248 °C (decomp.); Anal. Calcd for $C_{26}H_{41}N_5O_4 \cdot HCl \cdot 1.5H_2O$: C, 64.42; H, 6.76; N, 10.43. Found: C, 64.32; H, 6.64; N, 10.36.

EXAMPLE 82

10 4-(4-Methoxyphenyl)-4-phenylpiperidine. 4-Hydroxy-4-phenylpiperidine (5.00 g, 28.2 mmol, 1.00 equiv, Aldrich) was added to a suspension of $AlCl_3$ (18.8 g, 141 mmol, 5.00 equiv) in anhydrous anisole (100 mL). The mixture was stirred at room temperature for 1 hour and then
15 heated to 50 °C for 3.5 hours. It was cooled to room temperature and poured cautiously into ice-water. The mixture was basified to pH 11 by addition of 6 M aqueous NaOH, and extracted with EtOAc (3 x 75 mL). The combined organic solutions were applied directly to a flash
20 chromatography column, which was eluted with $CH_2Cl_2-NH_3$ in MeOH (0.67 M), 4:1 to afford 1.683 g (22%) of light yellow oil, which was characterized spectroscopically.

3-[4-(4-Methoxyphenyl)-4-phenylpiperidin-1-yl]propionitrile. Acrylonitrile (1.03 mL, 15.7 mmol, 2.50 equiv) was added at 0 °C to a solution of 4-(4-methoxyphenyl)-4-phenylpiperidine (1.68 g, 6.28 mmol, 1.00 equiv) in EtOH (20 mL) and the resulting solution was stirred for 1.5 hours at room temperature. After removal of the solvent,
30 the residue was purified by flash chromatography (SiO_2 , EtOAc- $CHCl_3$ 1:3) to give 1.41 g (70%) of colorless oil, which was characterized spectroscopically.

1-(3-Aminopropyl)-4-(4-methoxyphenyl)-4-phenylpiperidine.
35 To a stirred solution of 3-[4-(4-methoxyphenyl)-4-phenylpiperidin-1-yl]propionitrile (1.41 g, 4.40 mmol, 1.0 equiv) in anhydrous THF (10 mL) under argon was added a

solution of BH_3 in THF (1.0 M, 11.0 mL, 2.5 equiv) at room temperature. The mixture was refluxed for 4.5 hours and then cooled to room temperature. Aqueous HCl (6 N, 15 mL) was added and stirring was continued for 2 hours at 5 55-60 °C. The mixture was basified to pH 9 by addition of 6 N aq. NaOH and extracted with CH_2Cl_2 (3 x 75 mL). The combined organic solutions were dried over MgSO_4 and concentrated. The residue was dissolved in CH_2Cl_2 (10 mL) and treated with HCl in ether (1.0 M, 9.0 mL, 2.0 equiv). 10 The solvents were removed, ether (30 mL) was added, the mixture was filtered, and the filter cake was washed with ether (2 x 10 mL). Water (20 mL) was added to the resulting white solid, the pH was adjusted to 10 with 1 M NaOH, and the aqueous phase was extracted with CH_2Cl_2 (3 15 x 40 mL). The combined organic solutions were dried over MgSO_4 and concentrated to give 610 mg (43%) of white solid, which was characterized spectroscopically.

5-Carboxamide-2-ethyl-1,4-dihydro-3-{N-[3-(4-methoxyphenyl)-4-phenylpiperidin-1-yl]propyl}carboxamide- 20 6-methyl-4-(4-nitro)phenylpyridine hydrochloride hydrate (82). This compound was prepared according to Method B. Anhydrous CH_2Cl_2 (10 mL) was added to a mixture of 5-carboxamido-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.604 25 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (174 mg, 0.905 mmol, 1.50 equiv), and 4-(N,N-dimethylamino)pyridine (81 mg, 0.66 mmol, 1.1 equiv) and the resulting solution was stirred 30 for 1 hour at room temperature. A solution of 1-(3-aminopropyl)-4-(4-methoxyphenyl)-4-phenylpiperidine (234 mg, 0.721 mmol, 1.20 equiv) in CH_2Cl_2 (2 mL) was injected and the mixture was stirred at reflux for 6 hours. Methylene chloride (150 mL) was added and the organic 35 phase was washed with saturated aqueous ammonium chloride (2 x 40 mL), dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -

NH₃ in MeOH (0.77 M) 90:13) to afford 209 mg (55%) of yellow solid, which was characterized spectroscopically. To a solution of this product (200 mg, 0.310 mmol) in CH₂Cl₂ (10 mL) was added HCl in ether (1.0 M, 0.60 mL, 1.9 equiv). After removal of the solvents, the residue was dissolved in CH₂Cl₂ (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 150 mg of yellow solid: m.p. 183-184 °C; Anal. Calcd. for C₃₇H₄₃N₅O₅·HCl·1.25 H₂O: C, 63.78; H, 6.73; N, 10.05. Found: C, 63.80; H, 6.81; N, 9.72.

EXAMPLE 83

3-[4-(4-Chlorophenyl)-4-hydroxypiperidin-1-yl]propionitrile. Acrylonitrile (2.33 mL, 35.4 mmol, 2.50 equiv) was added at 0 °C to a solution of 4-(4-chlorophenyl)-4-hydroxypiperidine (3.00 g, 14.2 mmol, 1.00 equiv, Aldrich) in EtOH (30 mL) and the resulting solution was stirred for 1.5 hours at room temperature. The solvent was removed to give 3.71 g (99%) of white solid, which was characterized spectroscopically and used without purification for the next reaction.

1-(3-Aminopropyl)-4-(4-chlorophenyl)-4-hydroxypiperidine. To a stirred solution of 3-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]propionitrile (3.51 g, 13.2 mmol, 1.0 equiv) in anhydrous THF (20 mL) under argon was added a solution of BH₃ in THF (1.0 M, 46.4 mL, 3.5 equiv) at room temperature. The mixture was refluxed for 4.5 hours and then cooled to room temperature. Aqueous HCl (6 N, 30 mL) was added and stirring was continued for 2 hours at 55-60 °C. The mixture was basified to pH 9 by addition of 6 N aq. NaOH and extracted with CH₂Cl₂ (3 x 150 mL). The combined organic solutions were dried over MgSO₄ and concentrated. The residue was dissolved in CH₂Cl₂ (20 mL) and treated with HCl in ether (1.0 M, 27.7 mL, 2.1 equiv). The solvents were removed, ether (60 mL) was

added, the mixture was filtered, and the filter cake was washed with ether (2 x 20 mL). Water (40 mL) was added to the resulting white solid, the pH was adjusted to 10 with 1 M NaOH, and the aqueous phase was extracted with 5 CH_2Cl_2 (3 x 80 mL). The combined organic solutions were dried over MgSO_4 and concentrated to give 3.10 g (87%) of white solid, which was characterized spectroscopically.

5-Carboxamide-3-{N-[3-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)propyl]}carboxamide-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine hydrochloride (83). This compound was prepared according to Method B. Anhydrous CH_2Cl_2 (10 mL) was added to a mixture of 5-carboxamido-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.604 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (174 mg, 0.905 mmol, 1.50 equiv), and 4-(N,N-dimethylamino)pyridine (81 mg, 0.66 mmol, 1.1 equiv) and the resulting solution was stirred 20 for 1 hour at room temperature. A solution of 1-(3-aminopropyl)-4-(4-chlorophenyl)-4-phenylpiperidine (194 mg, 0.722 mmol, 1.20 equiv) in CH_2Cl_2 (2 mL) was injected and the mixture was stirred at reflux for 6 hours. Methylene chloride (150 mL) was added and the organic 25 phase was washed with saturated aqueous ammonium chloride (2 x 40 mL), dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , MeOH-EtOAc 1:3) to afford 71 mg (22%) of yellow solid, which was characterized spectroscopically. To a solution of 30 this product (56 mg, 0.10 mmol) in CH_2Cl_2 (3 mL) was added HCl in ether (1.0 M, 0.20 mL, 2.0 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (3 mL) and added dropwise to ether (20 mL) with swirling to give, after filtration, 57 mg of yellow solid: m.p. 178-35 179 °C; Anal. Calcd. for $\text{C}_{30}\text{H}_{34}\text{N}_5\text{O}_5 \cdot \text{HCl} \cdot 1.6 \text{CH}_2\text{Cl}_2$: C, 52.79; H, 5.64; N, 9.74. Found: C, 52.70; H, 5.89; N, 10.10.

EXAMPLE 84

3-(4-Benzylpiperidin-1-yl)propionitrile. Acrylonitrile (9.37 mL, 142 mmol, 2.50 equiv) was added at 0 °C to a solution of 4-benzylpiperidine (10.0 mL, 56.9 mmol, 1.00 equiv, Aldrich) in EtOH (60 mL) and the resulting solution was stirred for 1.5 hours at room temperature. The solvent was removed to give 12.98 g (99%) of colorless oil, which was characterized spectroscopically and used without purification for the next reaction.

1-(3-Aminopropyl)-4-benzylpiperidine. To a stirred solution of 3-(4-benzylpiperidin-1-yl)propionitrile (8.20 g, 35.9 mmol, 1.0 equiv) in anhydrous THF (20 mL) under argon was added a solution of BH_3 in THF (1.0 M, 126 mL, 3.5 equiv) at room temperature. The mixture was refluxed for 4.5 hours, then cooled to room temperature and concentrated to a volume of about 30 mL. Aqueous HCl (6 N, 80 mL) was added and stirring was continued for 2 hours at 55-60 °C. The mixture was basified to pH 9 by addition of 6 N aq. NaOH and extracted with CH_2Cl_2 (3 x 150 mL). The combined organic solutions were dried over MgSO_4 and concentrated. The residue was dissolved in CH_2Cl_2 (20 mL) and treated with HCl in ether (1.0 M, 75 mL, 2.1 equiv). The solvents were removed, ether (60 mL) was added, the mixture was filtered, and the filter cake was washed with ether (2 x 30 mL). Water (40 mL) was added to the resulting white solid, the pH was adjusted to 10 with 1 M NaOH, and the aqueous phase was extracted with CH_2Cl_2 (3 x 80 mL). The combined organic solutions were dried over MgSO_4 and concentrated to give 7.59 g (91%) of colorless oil, which was characterized spectroscopically.

5-Carboxanido-3-{N-[3-(4-benzylpiperidin-1-yl)propyl]}-carboxanido-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophonyl)pyridino hydrochloride hydrate octohydrate (84). This

compound was prepared according to Method B. Anhydrous CH_2Cl_2 (10 mL) was added to a mixture of 5-carboxamido-2-ethyl-1,4-dihydro-2-ethyl-6-methyl-4-(4-nitro-phenyl)pyridine-3-carboxylic acid (200 mg, 0.604 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (174 mg, 0.905 mmol, 1.50 equiv), and 4-(N,N-dimethylamino)pyridine (81 mg, 0.66 mmol, 1.1 equiv) and the resulting solution was stirred for 1 hour at room temperature. A solution of 1-(3-aminopropyl)-4-benzylpiperidine (181 mg, 0.779 mmol, 1.29 equiv) in CH_2Cl_2 (2 mL) was injected and the mixture was stirred at reflux for 6 hours. Methylene chloride (150 mL) was added and the organic phase was washed with saturated aqueous ammonium chloride (3 x 40 mL) and concentrated. A solution of the residue in EtOAc (100 mL) was extracted with 0.1 M aqueous HCl (2 x 100 mL) and the organic layer was discarded. The combined HCl solutions were basified to pH 10 by addition of 1 M aqueous NaOH and extracted with CH_2Cl_2 (3 x 100 mL). The combined CH_2Cl_2 solutions were dried over MgSO_4 and concentrated. A solution of the residue in CH_2Cl_2 (2 mL) was added dropwise into ether (20 mL) to afford, after filtration, 195 mg (60%) of yellow solid, which was characterized spectroscopically. To a solution of this product (183, 0.335 mmol) in CH_2Cl_2 (3 mL) was added HCl in ether (1.0 M, 0.65 mL, 1.9 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 190 mg of yellow solid: m.p. 163-164 °C; Anal. Calcd. for $\text{C}_{21}\text{H}_{29}\text{N}_5\text{O}_4 \cdot \text{HCl} \cdot \text{H}_2\text{O} \cdot 0.35 \text{ C}_6\text{H}_{10}\text{O}$: C, 62.14; H, 7.32; N, 11.18. Found: C, 62.15; H, 7.32; N, 11.11.

EXAMPLE 85

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1-(3-Aminopropyl)-4,4-dicyclohexylpiperidine. A solution of 3-(4,4-diphenylpiperidin-1-yl)propionitrile (1.01 g,

3.48 mmol, 1.00 equiv) in denatured EtOH (50 mL, 5% isopropanol) was stirred at 120-130 °C in the presence of 10% Pd on activated carbon (1.00 g, Aldrich) and hydrogen at 440 psi for 15 hours. The catalyst was filtered out
5 by use of Celite and washed with CH₂Cl₂ (100 mL) and MeOH (150 mL). After removal of the solvents, the residue was dissolved in CH₂Cl₂ (10 mL) and treated with HCl in ether (1.0 M, 8.7 mmol, 2.5 equiv). The solvents were removed again and the residue was recrystallized from hot EtOH-
10 ether (1:2). The white solid obtained from filtration of this mixture was taken up in water (40 mL), which was basified to pH 10 by addition of 1 N NaOH and extracted with CH₂Cl₂ (3 x 75 mL). The combined organic solutions were dried over MgSO₄ and concentrated to afford 650 mg of
15 colorless oil (61%), which was characterized spectroscopically.

5-Carboxamido-3-{N-[3-(4,4-dicyclohexylpiperidin-1-yl)-propyl]}carboxamide-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine hydrochloride hydrate octahydrate (85).
20 This compound was prepared according to Method B. Anhydrous CH₂Cl₂ (10 mL) was added to a mixture of 5-carboxamido-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.604 mmol, 1.00 equiv),
25 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (174 mg, 0.905 mmol, 1.50 equiv), and 4-(N,N-dimethylamino)pyridine (81 mg, 0.66 mmol, 1.1 equiv) and the resulting solution was stirred for 1 hour at room temperature. A solution of 1-(3-aminopropyl)-4,4-dicyclohexylpiperidine (181 mg, 0.779
30 mmol, 1.29 equiv) in CH₂Cl₂ (2 mL) was injected and the mixture was stirred at reflux for 6 hours. Methylene chloride (150 mL) was added and the organic phase was washed with saturated aqueous ammonium chloride (3 x 40
35 mL) and concentrated. A solution of the residue in EtOAc (100 mL) was extracted with 0.1 M aqueous HCl (2 x 100 mL) and the organic layer was discarded. The combined

HCl solutions were basified to pH 10 by addition of 1 M aqueous NaOH and extracted with CH_2Cl_2 (3 x 100 mL). The combined CH_2Cl_2 solutions were dried over MgSO_4 and concentrated. A solution of the residue in CH_2Cl_2 (2 mL) was added dropwise into ether (20 mL) to afford, after filtration, 242 mg (65%) of yellow solid, which was characterized spectroscopically. To a solution of this product (290, 0.470 mmol) in CH_2Cl_2 (10 mL) was added HCl in ether (1.0 M, 0.80 mL, 1.7 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 293 mg of yellow solid: m.p. 185-186 °C; Anal. Calcd. for $\text{C}_{36}\text{H}_{53}\text{N}_5\text{O}_4 \cdot \text{HCl} \cdot 0.75 \text{H}_2\text{O} \cdot 0.35 \text{C}_4\text{H}_{10}\text{O}$: C, 64.55; H, 8.33; N, 10.06. Found: C, 64.49; H, 8.62; N, 9.87.

EXAMPLE 86

4-Cyclohexylpiperidine. A solution of 4-phenylpyridine hydrochloride (4.50 g, 29.0 mmol, 1.00 equiv) in denatured EtOH (100 mL, 5% isopropanol) was stirred at 110-120 °C in the presence of 10% Pd on activated carbon (4.50 g, Aldrich) and hydrogen at 440 psi for 24 hours. The catalyst was filtered out by use of Celite and washed with CH_2Cl_2 (100 mL) and MeOH (150 mL). The filtrate was concentrated to give 5.32 g (90%) of white solid, which was characterized spectroscopically as 4-cyclohexylpiperidine hydrochloride. This white solid was taken up in water (150 mL), which was basified to pH 10 by addition of 1 N NaOH and extracted with CH_2Cl_2 (3 x 200 mL). The combined organic solutions were dried over MgSO_4 and concentrated to afford 4.27 g of white solid (88%), which was characterized spectroscopically.

3-(4-Cyclohexylpiperidin-1-yl)propionitrile. Acrylonitrile (4.16 mL, 63.1 mmol, 2.50 equiv) was added at 0 °C to a solution of 4-cyclohexylpiperidine (4.20 g,

25.3 mmol, 1.00 equiv) in EtOH (50 mL) and the resulting solution was stirred for 1.5 hours at room temperature. The solvent was removed to give 5.11 g (92%) of white solid, which was characterized spectroscopically and used without purification for the next reaction.

1-(3-Aminopropyl)-4-cyclohexylpiperidine. To a stirred solution of 3-(4-cyclohexylpiperidin-1-yl)propionitrile (5.11 g, 23.3 mmol, 1.0 equiv) in anhydrous THF (15 mL) under argon was added a solution of BH_3 in THF (1.0 M, 82 mL, 3.5 equiv) at room temperature. The mixture was refluxed for 4.5 hours, then cooled to room temperature and concentrated to a volume of about 30 mL. Aqueous HCl (6 N, 55 mL) was added and stirring was continued for 2 hours at 55-60 °C. The mixture was basified to pH 9 by addition of 6 N aq. NaOH and extracted with CH_2Cl_2 (3 x 100 mL). The combined organic solutions were dried over MgSO_4 and concentrated. The residue was dissolved in CH_2Cl_2 (20 mL) and treated with HCl in ether (1.0 M, 58 mL, 2.5 equiv). The solvents were removed, ether (40 mL) was added, the mixture was filtered, and the filter cake was washed with ether (2 x 20 mL). Water (40 mL) was added to the resulting white solid, the pH was adjusted to 10 with 1 M NaOH, and the aqueous phase was extracted with CH_2Cl_2 (3 x 80 mL). The combined organic solutions were dried over MgSO_4 and concentrated to give 4.63 g (88%) of colorless oil, which was characterized spectroscopically.

5-Carboxamide-3-{N-[3-(4-cyclohexylpiperidin-1-yl)propyl]}carboxamide-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine hydrochloride hydrate (86). This compound was prepared according to Method B. Anhydrous CH_2Cl_2 (10 mL) was added to a mixture of 5-carboxamido-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.604 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride

(174 mg, 0.905 mmol, 1.50 equiv), and 4-(*N,N*-dimethylamino)pyridine (81 mg, 0.66 mmol, 1.1 equiv) and the resulting solution was stirred for 1 hour at room temperature. A solution of 1-(3-aminopropyl)-4-cyclo-
 5 hexylpiperidine (175 mg, 0.780 mmol, 1.29 equiv) in CH_2Cl_2 (2 mL) was injected and the mixture was stirred at reflux for 6 hours. Methylene chloride (150 mL) was added and the organic phase was washed with saturated aqueous ammonium chloride (3 x 40 mL) and concentrated. A
 10 solution of the residue in EtOAc (100 mL) was extracted with 0.1 M aqueous HCl (2 x 100 mL) and the organic layer was discarded. The combined HCl solutions were basified to pH 10 by addition of 1 M aqueous NaOH and extracted with CH_2Cl_2 (3 x 100 mL). The combined CH_2Cl_2 solutions
 15 were dried over MgSO_4 and concentrated. A solution of the residue in CH_2Cl_2 (2 mL) was added dropwise into ether (20 mL) to afford, after filtration, 203 mg (63%) of yellow solid, which was characterized spectroscopically. To a
 20 solution of this product (257, 0.478 mmol) in CH_2Cl_2 (10 mL) was added HCl in ether (1.0 M, 0.90 mL, 1.9 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 260 mg of yellow
 25 solid: m.p. 167-168 °C; Anal. Calcd. for $\text{C}_{30}\text{H}_{43}\text{N}_5\text{O}_4 \cdot \text{HCl} \cdot 0.75 \text{ H}_2\text{O}$: C, 61.32; H, 7.80; N, 11.92. Found: C, 61.16; H, 8.06; N, 11.54.

EXAMPLE 87

30 3-[*N*-(3-Bromopropyl)]carboxamide-5-carboxamide-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine. This compound is prepared according to Method B. Anhydrous CH_2Cl_2 (10 mL) is added to a mixture of 5-carboxamido-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-
 35 carboxylic acid (200 mg, 0.604 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (174 mg, 0.905 mmol, 1.50 equiv), and 4-(*N,N*-dimethyl-

amino)pyridine (81 mg, 0.66 mmol, 1.1 equiv) and the resulting solution is stirred for 1 hour at room temperature. To this solution is added a CH_2Cl_2 solution (10 mL) of 3-bromopropylamine, which is generated from 3-bromopropylamine hydrobromide (172 mg, 0.785 mmol, 1.30 equiv) by stirring for 10 minutes over solid K_2CO_3 followed by filtration. The reaction mixture is stirred at room temperature for 24 hours. Methylene chloride (150 mL) is added and the organic phase is washed with 0.1 M aqueous HCl (3 x 40 mL), dried over MgSO_4 and concentrated. A solution of the residue in CH_2Cl_2 (2 mL) is added dropwise into ether (20 mL). The solid product is obtained by filtration and characterized spectroscopically.

3-{N-[3-(4-acetyl-4-phenylpiperidin-1-yl)propyl]}carboxamide-5-carboxamide-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine (37). A suspension of 4-acetyl-4-phenylpiperidine hydrochloride (63.7 mg, 0.266 mmol, 1.20 equiv), 3-[N-(3-bromopropyl)]carboxamido-5-carboxamido-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine (100 mg, 0.222 mmol, 1.00 equiv), potassium carbonate (92.0 mg, 0.666 mmol, 3.00 equiv), and potassium iodide (18.4 mg, 0.111 mmol, 0.50 equiv) in acetone (1.1 mL) is stirred at reflux under argon for 15 hours. The mixture is cooled to room temperature and concentrated. The residue is diluted with EtOAc (20 mL) and extracted with 0.1 M aqueous HCl (3 x 30 mL). The combined aqueous solutions are basified by addition of 1 M aqueous NaOH and extracted with CH_2Cl_2 (3 x 50 mL). The combined CH_2Cl_2 solutions are dried over MgSO_4 and concentrated to afford the product, which is purified by flash chromatography and characterized spectroscopically.

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EXAMPLE 38

2-Ethyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-{N-[3-

(4,4-diphenylpiperidin-1-yl)propyl}}carboxamidopyridino-5-carboxylic acid. A mixture of 2.15 g of 5-benzoyloxycarbonyl-2-ethyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl}}carboxamidopyridine (3.08 mmol) and 0.510 g of 10% Pd/C in 50 mL of methanol was hydrogenated using a balloon method for 6 h, filtered through Celite 545, and the residue was washed with methanol (4 X 30 mL). The combined filtrates were concentrated to give 1.76 g (96%) of yellow solid, which was used in the next step without any further purification.

2-Ethyl-1,4-dihydro-6-methyl-5-(O-methylhydroxamyl)carboxyl-4-(4-nitro)phenyl-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl}}carboxamidopyridine dihydrochloride salt (88). This compound was prepared according to Method D. A mixture of 173 mg of 2-ethyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl}}carboxamidopyridine-5-carboxylic acid (0.284 mmol), 38.2 mg of DMAP (0.312 mmol), and 87.9 mg of DCC (0.426 mmol) in 10 mL of dry dichloromethane was stirred at room temperature for 1 h. O-Methylhydroxylamine hydrochloride (71.2 mg, 0.852 mmol) and 45.2 mg of sodium carbonate (0.426 mmol) were added and stirring was continued for 4 days. The mixture was filtered and concentrated, and the residue was dissolved in 50 mL of ethyl acetate. This solution was washed with 30 mL of saturated sodium bicarbonate solution, dried (Na_2CO_3), and concentrated. The residue was chromatographed on 200 g of silica packed with 5% MeOH-EtOAc. The column was eluted with 5% (0.5 L), 10% (0.5 L), 15% (0.5 L), 20% (1 L), and 25% (1 L) to give 20 mg (11%) of yellow solid, which was characterized spectroscopically. A solution of this free base (20 mg) in 0.5 mL of dichloromethane was added to 1 M HCl in ether (2 mL). The precipitate was collected, washed with 5 mL of ether, and dried: mp 196-200 °C; Anal. Calcd for $\text{C}_{37}\text{H}_{43}\text{N}_5\text{O}_5 \cdot \text{HCl} \cdot 0.9 \text{CH}_2\text{Cl}_2$: C, 60.64; H, 6.15; N, 9.33. Found:

C, 60.89; H, 5.63; N, 9.30.

EXAMPLE 89

5 3-Ethoxycarbonyl-2-(ethoxycarbonyl)methyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine. A stirred solution of 2.02 g of diethyl 1,3-acetonedicarboxylate (10.0 mmol), 1.15 g of methyl 3-aminocrotonate (10.0 mmol), and 1.51 g of 4-nitrobenzaldehyde (10.0 mmol) in 100 mL of isopropanol was heated at reflux temperature for 3 days, cooled, and the solvent was removed in vacuo. The crude product was chromatographed on 200 g of silica packed with 5% EtOAc-hexanes. The column was eluted with 5% to 50% EtOAc-hexanes (5% change/500 mL) to afford 2.71 g of yellow viscous oil: Anal. Calcd for $C_{21}H_{24}N_2O_8$: C, 58.23; H, 5.59; N, 6.48. Found: C, 58.17; H, 5.76; N, 6.25.

3-Ethoxycarbonyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carbamide)methylpyridine, fumarate salt (89). A solution of 803 mg of 3-ethoxycarbonyl-2-(ethoxycarbonyl)methyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine (1.86 mmol) and 98 mg of NaOH (2.5 mmol) in 10 mL of 1:1 dioxane-water mixture were stirred at room temperature for 24 hrs, concentrated to a small volume, partitioned between water (10 mL) and ethyl acetate (20 mL), separated, and the aqueous layer was washed with ether (20 mL). The aqueous extract was acidified with concentrated HCl (pH = 2-3), the precipitated oil was extracted with 20 mL of EtOAc, dried (Na_2SO_4), and the solvent was removed in vacuo to afford 750 mg of 3-(carboxy)methyl-2-(ethoxycarbonyl)methyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine (99.8%). The crude acid was used in the next step without any further purification.

Dicyclohexylcarbodiimide (164 mg, 0.796 mmol) was added, in one portion, to a stirred solution of 354 mg of 3-(carboxy)methyl-2-(ethoxycarbonyl)methyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine (0.875 mmol) and 225 mg of 1-(3-aminopropyl)-4,4-diphenylpiperidine (0.796 mmol) in 5 mL of dry dichloromethane. Stirring was continued at room temperature for 18 h. The solvent was removed in vacuo, the residue was triturated with ether (10 mL), and the mixture was filtered. The solid was washed with ether (2 x 10 mL) and the filtrate was concentrated. The crude product was chromatographed on 150 g of silica packed with 10% MeOH-EtOAc. The column was eluted with 10% to 25% MeOH-EtOAc (5% change/500 mL) to afford 273 mg of product: Anal. Calcd for $C_{39}H_{44}N_4O_7 \cdot 0.5EtOAc$: C, 67.91; H, 6.58; N, 8.12. Found: C, 67.88; H, 6.51; N, 8.13.

Fumarate Salt: A mixture of 51.0 mg of 3-ethoxycarbonyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)methylpyridine (0.0749 mmol) and 8.7 mg of fumaric acid (0.0749 mmol) in 2 mL of 1:1 acetone-water was heated to boiling until a homogeneous solution resulted. The reaction mixture was cooled, filtered, and the solvent was removed in vacuo to give 58.5 mg of yellow solid (98%): mp 134-137 °C; Anal. Calcd for $C_{43}H_{46}N_4O_{11}$: C, 64.81; H, 6.07; N, 7.03. Found: C, 64.61; H, 6.14; N, 6.91.

EXAMPLES 90 AND 91

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2-Chloroethoxy-3-ethoxycarbonyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenylpyridine. A stirred mixture of 1.64 g of ethyl 4-chloro-3-oxobutyrate (10.0 mmol), 1.15 g of ethyl 3-aminocrotonate (10.0 mmol), and 1.51 g of 4-nitrobenzaldehyde (10.0 mmol) in 100 mL of methanol was heated at reflux temperature for 18 hrs, cooled, and the solvent was removed in vacuo.

The crude product was initially chromatographed on 200 g of silica packed with dichloromethane and eluted with dichloromethane to 5% EtOAc-dichloromethane (1% change/500 mL) to afford a yellow oily solid which was approximately 50% pure by ¹H NMR spectroscopy. This was rechromatographed on 200 g of silica packed with EtOAc-hexanes (1:4). The column was eluted with 600 mL of 1:4 EtOAc-hexanes and 1 L of 1:3 EtOAc-hexanes to afford 590 mg of the desired product (15%) as an oily yellow solid: The chromatographed product was used in the next alkylation step without any further characterization (unstable product, kept in the freezer).

3-Ethoxycarbonyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)amino)methylpyridine, hydrochloride (90)
 1,4,7,7-Tetrahydro-3-methoxycarbonyl-6-methyl-5-oxo-4-(4-nitrophenyl)-6-(3-(4,4-diphenylpiperidin-1-yl))propylpyrrolo[3,4-b]pyridine, hydrochloride salt, (91). A stirred solution of 93 mg of 1-(3-aminopropyl)-4,4-diphenylpiperidine (0.33 mmol), 118 mg of 5-methyl-2-chloromethyl-4-(4-nitrophenyl)-3-carboethoxy-5-carbomethoxy-1,4-dihydropyridine (0.299 mmol), and 182 mg of potassium carbonate (1.32 mmol) in 5 mL of dry DMF were stirred at room temperature for 6 days. Ethyl acetate (30 mL) was added, and the organic solution was washed with water (20 mL + 2 x 10 mL), dried (Na₂SO₄), and concentrated. The crude product was chromatographed on 100 g of silica packed with MeOH-isopropyl amine-EtOAc (1:1:98). The column was eluted with MeOH-isopropyl amine-EtOAc (1:1:98 (0.5 L), 2:1:97 (0.5 L), 5:1:94 (2 L), 20:1:79 (2 L) to give 63 mg of the 3-ethoxycarbonyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)amino)methylpyridine, hydrochloride (32%) and 16 mg of 1,4,7,7-Tetrahydro-3-methoxycarbonyl-6-methyl-5-oxo-4-(4-nitrophenyl)-6-(3-(4,4-diphenylpiperidin-1-yl))propylpyrrolo[3,4-b]pyridine,

hydrochloride salt (9%).

Hydrochloride Salts: The hydrochloride salts were prepared by dissolving the free bases in minimum amounts of ethyl acetate (0.5 mL) and addition of an excess of 1 M HCl in ether (1 mL). Compound 90 can exist as a monohydrochloride or as a dihydrochloride salt. The monohydrochloride salt is soluble in ethyl acetate and the dihydrochloride salt is not. The two can be separated by trituration of the crude product with ethyl acetate, in which case, the monohydrochloride can be found in the ethyl acetate extract.

3-Ethoxycarbonyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitro)phenyl-2-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)amino)methylpyridine, hydrochloride hydrate (90):

Anal. Calcd for $C_{39}H_{44}N_4O_7 \cdot HCl \cdot H_2O$: C, 63.71; H, 6.44; N, 7.62. Found: C, 63.75; H, 6.53; N, 7.19.

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3-Ethoxycarbonyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-2-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)amino)methylpyridine, dihydrochloride:

Anal. Calcd for $C_{39}H_{44}N_4O_7 \cdot 2HCl$: C, 62.15; H, 6.15; N, 7.43. Found: C, 61.75; H, 6.16; N, 7.32.

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1,4,7,7-Tetrahydro-3-methoxycarbonyl-6-methyl-5-oxo-4-(4-nitrophenyl)-6-(3-(4,4-diphenylpiperidin-1-yl))propylpyrrolo[3,4-b]pyridine, hydrochloride hydrate (91).

Anal. Calcd for $C_{37}H_{38}N_4O_6 \cdot HCl \cdot H_2O$: C, 64.48; H, 6.00; N, 8.13. Found: C, 64.05; H, 6.05; N, 8.53.

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EXAMPLE 92

1,4-Dihydro-5-methoxycarbonyl-1,2,6-trimethyl-4-(4-nitrophenyl)-3-[3-(4,4-diphenylpiperidin-1-yl)propoxy]carbonylpyridine hydrochloride hydrate (92). Sodium hydride

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(60% dispersion in mineral oil, 100 mg, 2.51 mmol, 3.0 equiv) was washed with anhydrous hexane under argon, and the washings were discarded. Tetrahydrofuran (11 mL) was added and the resulting suspension was cooled to 0 °C.

5 A solution of 1,4-dihydro-5-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophenyl)-3-[3-(4,4-diphenylpiperidin-1-yl)propoxy]carbonylpyridine (510 mg, 0.840 mmol, 1.0 equiv) in THF (4 mL) was added, followed by CH₃I (0.156 mL, 2.51 mmol, 3.0 equiv). The resulting orange

10 suspension was stirred at 0 °C for 2 hours and then at room temperature for 1.5 hours. Water (10 mL) was added, the pH was adjusted to 9-10 by addition of 6 M aq. NaOH, and the aqueous phase was extracted with EtOAc (4 x 20 mL). The combined organic solutions were dried over MgSO₄

15 and concentrated. The residue was purified by flash chromatography (SiO₂, EtOAc-hexane 1:1 to 1:0) to give 218 mg (42%) of yellow solid, which was characterized spectroscopically. To a solution of this product in EtOAc (5 mL) was added a solution of HCl in ether (1.0 M,

20 0.38 mL, 1.1 equiv). The mixture was warmed to 50 °C until the solution was clear, then cooled slowly to 0 °C. Filtration afforded 64 mg of yellow solid: m.p. 127-128 °C; Anal. Calcd. for C₃₇H₃₄N₄O₆·HCl·H₂O: C, 65.53; H, 6.54; N, 6.20. Found: C, 65.73; H, 6.34; N, 6.12.

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EXAMPLE 93

(±)-1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carbamidopyridine hydrochloride hydrate ((±)-93). This compound was prepared according to Method

30 A. A solution of N-(3-(4,4-diphenylpiperidin-1-yl)propyl)acetacetamide (365 mg, 0.964 mmol, 1.0 equiv), methyl 3-aminocrotonate (138 mg, 1.20 mmol, 1.2 equiv, Aldrich), and 4-nitrobenzaldehyde (181 mg, 1.20 mmol, 1.2 equiv, Aldrich) in isopropanol (20 mL) was refluxed under argon for 60 hours. The mixture was cooled to room

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- temperature and concentrated, and the residue was diluted with CH_2Cl_2 , washed with water, dried over MgSO_4 , and concentrated. The residue was purified by flash chromatography (SiO_2 , EtOAc, followed by EtOAc-MeOH 19:1 and 9:1) to give 147.8 mg (25%) of yellow solid, which was characterized spectroscopically. To a solution of this product in EtOH (2 mL) was added a solution of HCl in ether (1.0 M, 0.24 mL, 1.0 equiv). Addition of ethyl acetate (3 mL) followed by heating gave a clear solution.
- Slow cooling of this solution, followed by filtration, gave 91 mg of yellow crystalline solid: m.p. 182-183 °C; Anal. Calcd. for $\text{C}_{23}\text{H}_{40}\text{N}_4\text{O}_3 \cdot \text{HCl} \cdot \text{H}_2\text{O}$: C, 65.20; H, 6.54; N, 8.45. Found: C, 65.30; H, 6.28; N, 8.15.
- (-)- and (+)-93 hydrochloride hydrate. The enantiomers of 93·HCl·H₂O were separated on a chiral HPLC column as follows. Four injections of (±)-93·HCl·H₂O (ca. 22.5 mg per injection in EtOH solution) were made onto a Chiralpak AS column (20 x 250 mm, Daicel), which was eluted with EtOH-hexane-diethylamine (30:70:0.05) at a flowrate of 3.0 mL/min with UV detection at 300 nm. The first major peak to elute (retention time 8.68 min) was further purified by flash chromatography (SiO_2 , MeOH- CH_2Cl_2 12:88). To a solution of this product in CH_2Cl_2 (3 mL) was added HCl in ether (1.0 M, 0.25 mL). After removal of the solvents, a solution of the residue in CH_2Cl_2 (2 mL) was added dropwise into ether (6 mL) with swirling to give, after filtration, 18.6 mg of yellow powder: $[\alpha]_D = -30.4^\circ$ (CH_2Cl_2 , 0.000745 g/mL); m.p. 176 °C; Anal. Calcd. for $\text{C}_{23}\text{H}_{40}\text{N}_4\text{O}_3 \cdot \text{HCl} \cdot \text{H}_2\text{O}$: C, 65.20; H, 6.54; N, 8.45. Found: C, 65.36; H, 6.46; N, 8.42. The second major peak to elute from the chiral column (retention time 14.14 min) was reinjected into the chiral column, collected, and converted to the HCl salt and precipitated as described for the (-)- enantiomer to afford 8.5 mg of yellow powder: $[\alpha]_D = +26.6^\circ$ (CH_2Cl_2 , 0.001033 g/mL); m.p. 182 °C; Anal. Calcd. for $\text{C}_{23}\text{H}_{40}\text{N}_4\text{O}_3 \cdot \text{HCl} \cdot \text{H}_2\text{O}$: C, 65.20; H, 6.54;

N, 8.45. Found: C, 65.51; H, 6.42; N, 8.36.

EXAMPLE 94

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(4-nitrophonyl)-3-[3-(4,4-diphenylpiperidin-1-yl)propoxy]carbonylpyridino hydrochloride (94). This compound was prepared according to Method A. A solution of methyl 3-aminocrotonate (265 mg, 2.3 mmol, 1.0 equiv), 4-nitrobenzaldehyde (348 mg, 2.3 mmol, 1.0 equiv), and acetoacetic acid 3-[4,4-diphenylpiperidin-1-yl]propyl ester (872 mg, 2.3 mmol, 1.0 equiv) in isopropanol was refluxed under argon with stirring for 68 hours. Cooling and removal of solvent gave a residue, which was purified by flash chromatography (SiO₂, EtOAc-hexane 1:1 and 1:2 followed by EtOAc) to afford 717 mg (51%) of yellow solid, which was characterized spectroscopically. To a solution of this product (710 mg, 1.16 mmol, 1.0 equiv) in EtOH (5 mL) was added a solution of HCl in ether (1.0 M, 1.5 mL, 1.5 mmol, 1.3 equiv). The solvents were removed and the residue was dissolved in CH₂Cl₂. This solution was added dropwise to 25 mL of ether to afford, after filtration, 500 mg of yellow crystalline solid: m.p. 152-153 °C. Anal. Calcd. for C₃₅H₃₉N₃O₆·HCl: C, 66.92; H, 6.24; N, 6.50. Found: C, 66.70; H, 5.99; N, 6.27.

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EXAMPLE 95

5-Carboxamide-1,4-dihydro-2,6-dimethyl-4-(4-nitrophonyl)pyridino-3-carboxylic acid. A solution of 3-aminocrotonamide (6.028 g, 60.21 mmol), 4-nitrobenzaldehyde (6.066 g, 40.14 mmol) and 2-cyanoethyl acetoacetate (6.227 g, 40.14 mmol) in 125 mL of EtOH was refluxed for 48 hrs. The reaction mixture was filtered and the filtrate was concentrated to give a brown oil. This brown oil was dissolved in 250 mL of CHCl₃ (with addition of a small amount of acetone to give a homogeneous solution), washed with water (2 x 100 mL) and

dried over Na_2SO_4 . After filtration and removal of solvent, the residue was dissolved into 200 mL of MeOH and treated with 100 mL 2N KOH solution at 0 °C for 30 min. The MeOH was removed in vacuo and the aqueous layer
5 was diluted with 100 mL of water and washed with EtOAc (2 x 100 mL). With stirring, the aqueous layer was acidified to pH 1 by addition of 6 N hydrochloric acid. The yellow precipitate was collected by filtration, washed with 10 mL of cold water and dried in vacuo to afford 5.877 g
10 (46.1% yield for two steps) of yellow powder.

3-(4-Hydroxy-4-phenylpiperidin-1-yl)propionitrile. To a solution of 4-hydroxy-4-phenylpiperidine (3.11 g, 17.5 mmol, 1.00 equiv) in EtOH (30 mL) was added acrylonitrile
15 (2.89 mL, 43.8 mmol, 2.50 equiv) dropwise at 0 °C. The mixture was stirred at room temperature for 1.5 hours and then concentrated to afford 3.71 g (92%) of white solid, which was characterized spectroscopically.

20 1-(3-Aminopropyl)-4-hydroxy-4-phenylpiperidine. To a solution of 3-(4-hydroxy-4-phenylpiperidin-1-yl)propionitrile (3.71 g, 16.1 mmol, 1.00 equiv) in THF (15 mL) at room temperature was added borane-tetrahydrofuran complex (1.0 M in THF, 56.3 mL, 56.3
25 mmol, 3.50 equiv) dropwise. The mixture was stirred at reflux for 4.5 hours and then cooled to room temperature. Aqueous HCl (6 N, 85 mL) was added and the mixture was stirred at 50-70 °C for 2 hours. The mixture was basified to pH 9-10 by addition of 6 N aqueous NaOH and extracted
30 with EtOAc (75 mL) and CH_2Cl_2 (3 x 75 mL). The combined organic solutions were dried over MgSO_4 and concentrated. To a solution of the residue in CH_2Cl_2 (75 mL) was added HCl in Et_2O (1.0 M, 38 mL, 2.3 equiv). After removal of the solvents, the residue was triturated with Et_2O (185
35 mL). The resulting white solid was collected by filtration and washed with Et_2O . Water (50 mL) was added to this solid, and the mixture was basified to pH 10-11

by addition of 1 N aqueous NaOH and extracted with CH_2Cl_2 (150 mL + 2 x 75 mL). The combined CH_2Cl_2 solutions were dried over MgSO_4 and concentrated to give 3.12 g (83%) of colorless oil, which was characterized spectroscopically.

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5-Carboxamido-1,4-dihydro-3-{N-[3-(4-hydroxy-4-phenylpiperidin-1-yl)propylcarboxamide]}-2,6-dimethyl-4-(4-nitrophenyl)pyridine hydrochloride hydrate (95). A mixture of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.63 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (181.3 mg, 0.946 mmol, 1.50 equiv) and 4-dimethylaminopyridine (84.7 mg, 0.690 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (15 mL) was stirred at room temperature under argon for 1 hour. A solution of 1-(3-aminopropyl)-4-hydroxy-4-phenylpiperidine (177 mg, 0.756 mmol, 1.20 equiv) in CH_2Cl_2 (10 mL) was injected, and the mixture was stirred at reflux for 14 hours. Anhydrous DMF (8 mL) was injected, and the resulting clear solution was refluxed for an additional hour. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (150 mL), and washed with saturated aqueous NH_4Cl (3 x 40 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH-methanolic ammonia (2 M) 100:9:7) to afford 145 mg (43%) of 95 free base as a yellow solid, which was characterized spectroscopically. To a solution of this product in CH_2Cl_2 (10 mL) was added HCl in ether (1.0 M, 0.5 mL, 1.3 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 130 mg of yellow solid: m.p. 159 °C (decomp.); Anal. Calcd. for $\text{C}_{27}\text{H}_{35}\text{N}_5\text{O}_5 \cdot \text{HCl} \cdot 1.9 \text{H}_2\text{O}$: C, 57.64; H, 6.64; N, 11.59. Found: C, 57.50; H, 6.65; N, 11.58.

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4-Acetyl-1-(3-aminopropyl)-4-phenylpiperidine. 4-Acetyl-4-phenylpiperidine (1.53 g, 7.50 mmol, 1.00 equiv, Aldrich), 3-bromopropylamine hydrobromide (1.64 g, 7.50 mmol, 1.00 equiv) and potassium carbonate (1.24 g, 9.00 mmol, 1.20 equiv) were stirred in refluxing 1,4-dioxane (50 mL) for 12 hours. After removal of dioxane, water (50 mL) was added and the pH was adjusted to 11-12 by addition of 1 N aqueous NaOH. The mixture was extracted with CH₂Cl₂ (100 mL + 3 X 50 mL). The combined organic solutions were dried over MgSO₄ and concentrated. The residue was purified by flash chromatography (EtOAc-MeOH-Et₃N 100:40:20) to give 780 mg (40%) of colorless oil, which was characterized spectroscopically.

3 - { N - [3 - (4 - A c e t y l - 4 - p h e n y l p i p e r i d i n - 1 - y l) p r o p y l] } c a r b o x a m i d e - 5 - c a r b o x a m i d e - 1 , 4 - d i h y d r o - 2 , 6 - d i m e t h y l - 4 - (4 - n i t r o p h e n y l) p y r i d i n e h y d r o c h l o r i d e c o n s e q u i h y d r a t e (96). A mixture of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine hydrochloride (200 mg, 0.63 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (181.3 mg, 0.946 mmol, 1.50 equiv) and 4-dimethylaminopyridine (84.7 mg, 0.690 mmol, 1.10 equiv) in anhydrous CH₂Cl₂ (20 mL) was stirred at room temperature under argon for 1 hour. A solution of 4-acetyl-1-(3-aminopropyl)-4-phenylpiperidine (197 mg, 0.756 mmol, 1.20 equiv) in CH₂Cl₂ (10 mL) was injected, and the mixture was stirred at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH₂Cl₂ (150 mL), and washed with saturated aqueous NH₄Cl (3 x 40 mL). The organic phase was dried over MgSO₄ and concentrated. The residue was purified by flash chromatography (SiO₂, CHCl₃-MeOH-methanolic ammonia (2 M) 90:8:5) to afford 220 mg (62%) of 96 free base as a yellow solid, which was characterized spectroscopically. To a solution of this product in CH₂Cl₂ (10 mL) was added HCl in ether (1.0 M, 0.5 mL, 1.3 equiv). After removal

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of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 190 mg of 96 hydrochloride sesquihydrate (yellow solid): m.p. 177 °C (decomp.);

5 Anal. Calcd. for $\text{C}_{21}\text{H}_{27}\text{N}_5\text{O}_5 \cdot \text{HCl} \cdot 1.5 \text{H}_2\text{O} \cdot 0.1 \text{Et}_2\text{O}$: C, 59.79; H, 6.71; N, 11.10. Found: C, 59.86; H, 6.73; N, 10.88.

EXAMPLE 97

1-(3-Aminopropyl)-4-cyano-4-phenylpiperidine. 4-Cyano-4-phenylpiperidine hydrochloride (5.01 g, 22.5 mmol, 1.00 equiv, Aldrich) was added to water (100 mL), and the solution was basified to pH 10-11 by addition of 6 N aqueous NaOH. The aqueous phase was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic solutions were dried

15 over MgSO_4 and concentrated. To the residue were added 3-bromopropylamine hydrobromide (4.92 g, 22.5 mmol, 1.00 equiv, Aldrich), anhydrous K_2CO_3 (3.42 g, 24.8 mmol, 1.10 equiv), and 1,4-dioxane (100 mL). The mixture was stirred at reflux for 24 hours under a CaSO_4 drying tube.

20 The solvent was removed, and the product was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH-methanolic ammonia (2 M) 100:8:4 to 100:20:8) to give 3.23 g (59%) of colorless oil, which was characterized spectroscopically.

25 (±)-5-Carboxamide-3-{N-[3-(4-cyano-4-phenylpiperidin-1-yl)propyl]}carboxamide-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine hydrochloride sesquihydrate (97). A mixture of 5-carboxamide-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.63 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (181.3 mg, 0.946 mmol, 1.50 equiv) and 4-dimethylaminopyridine (84.7 mg, 0.690 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (20 mL) was stirred at room temperature under argon for 1 hour. A solution

35 of 1-(3-aminopropyl)-4-cyano-4-phenylpiperidine (184 mg, 0.756 mmol, 1.20 equiv) in CH_2Cl_2 (10 mL) was injected, and the mixture was stirred at reflux for 6 hours. The

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mixture was cooled to room temperature, diluted with CH_2Cl_2 (150 mL), and washed with saturated aqueous NH_4Cl (3 x 40 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash
5 chromatography (SiO_2 , CHCl_3 -MeOH-methanolic ammonia (2 M) 100:4:2) to afford 220 mg (64%) of 97 free base as a yellow solid, which was characterized spectroscopically. To a solution of this product (210 mg, 0.387 mmol) in CH_2Cl_2 (10 mL) was added HCl in ether (1.0 M, 0.5 mL, 1.3
10 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 200 mg of 97 hydrochloride sesquihydrate (yellow solid): m.p. 182 °C (decomp.); Anal. Calcd. for $\text{C}_{20}\text{H}_{24}\text{N}_6\text{O}_4 \cdot \text{HCl} \cdot 1.5 \text{ H}_2\text{O}$: C, 59.45; H, 6.32; N, 13.87. Found: C, 59.35; H, 6.15; N, 13.76.

(-)- and (+)-97 hydrochloride hydrate. The enantiomers of 3 free base (700 mg) were separated in seven
20 injections on a Chiralpak AS column (20 x 250 mm, Daicel), which was eluted with EtOH-hexane 20:80 at 9.0 mL/min with UV detection at 300 nm. The first major peak eluted at 27 min. To a solution of this product ($[\alpha]_D = +29.9^\circ$ (MeOH, 0.01395 g/mL)) in EtOH (10 mL) was added
25 HCl in ether (1.0 M, 0.50 mL) at 0 °C. After removal of the solvents, a solution of the residue in EtOH (2 mL) was added dropwise into ether (50 mL) with swirling to give, after filtration, 282.1 mg of yellow powder: $[\alpha]_D = -45.0^\circ$ (MeOH, 0.0119 g/mL); m.p. 199 °C (decomp.);
30 Anal. Calcd. for $\text{C}_{20}\text{H}_{24}\text{N}_6\text{O}_4 \cdot \text{HCl} \cdot 2.15 \text{ H}_2\text{O}$: C, 58.32; H, 6.41; N, 13.60. Found: C, 58.49; H, 6.22; N, 13.31. The second major component eluted at 43 min ($[\alpha]_D = -28.7^\circ$ (MeOH, 0.02005 g/mL)). This product was converted to the HCl salt and precipitated as described for the other
35 enantiomer to afford 272.9 mg of yellow powder: $[\alpha]_D = +45.3^\circ$ (MeOH, 0.01085 g/mL); m.p. 199 °C (decomp.); Anal. Calcd. for $\text{C}_{20}\text{H}_{24}\text{N}_6\text{O}_4 \cdot \text{HCl} \cdot 2.15 \text{ H}_2\text{O}$: C, 58.32; H, 6.41; N,

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13.60. Found: C, 58.16; H, 6.21; N, 13.39.

EXAMPLE 98

5 4-(4-Methoxyphenyl)-4-phenylpiperidino. 4-Hydroxy-4-phenylpiperidine (5.00 g, 28.2 mmol, 1.00 equiv, Aldrich) was added to a suspension of AlCl_3 (18.8 g, 141 mmol, 5.00 equiv) in anhydrous anisole (100 mL). The mixture was stirred at room temperature for 1 hour and then heated to
10 50 °C for 3.5 hours. It was cooled to room temperature and poured cautiously into ice-water. The mixture was basified to pH 11 by addition of 6 M aqueous NaOH, and extracted with EtOAc (3 x 75 mL). The combined organic solutions were applied directly to a flash chromatography
15 column, which was eluted with $\text{CH}_2\text{Cl}_2\text{-NH}_3$ in MeOH (0.67 M), 4:1 to afford 1.683 g (22%) of light yellow oil, which was characterized spectroscopically.

3-[4-(4-Methoxyphenyl)-4-phenylpiperidin-1-yl]propionitrile. Acrylonitrile (1.03 mL, 15.7 mmol, 2.50 equiv) was added at 0 °C to a solution of 4-(4-methoxyphenyl)-4-phenylpiperidine (1.68 g, 6.28 mmol, 1.00 equiv) in EtOH (20 mL) and the resulting solution was stirred for 1.5 hours at room temperature. After
25 removal of the solvent, the residue was purified by flash chromatography (SiO_2 , EtOAc- CHCl_3 , 1:3) to give 1.41 g (70%) of colorless oil, which was characterized spectroscopically.

30 1-(3-Aminopropyl)-4-(4-methoxyphenyl)-4-phenylpiperidino. To a stirred solution of 3-[4-(4-methoxyphenyl)-4-phenylpiperidin-1-yl]propionitrile (1.41 g, 4.40 mmol, 1.0 equiv) in anhydrous THF (10 mL) under argon was added a solution of BH_3 in THF (1.0 M, 11.0 mL, 2.5 equiv) at
35 room temperature. The mixture was refluxed for 4.5 hours and then cooled to room temperature. Aqueous HCl (6 N, 15 mL) was added and stirring was continued for 2 hours

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at 55-60 °C. The mixture was basified to pH 9 by addition of 6 N aqueous NaOH and extracted with CH₂Cl₂ (3 x 75 mL). The combined organic solutions were dried over MgSO₄ and concentrated. The residue was dissolved in
5 CH₂Cl₂ (10 mL) and treated with HCl in ether (1.0 M, 9.0 mL, 2.0 equiv). The solvents were removed, ether (30 mL) was added, the mixture was filtered, and the filter cake was washed with ether (2 x 10 mL). Water (20 mL) was added to the resulting white solid, the pH was adjusted
10 to 10 with 1 M NaOH, and the aqueous phase was extracted with CH₂Cl₂ (3 x 40 mL). The combined organic solutions were dried over MgSO₄ and concentrated to give 610 mg (43%) of white solid, which was characterized spectroscopically.

15

5-Carboxamido-1,4-dihydro-3-{N-[3-(4-(4-methoxyphenyl)-4-phenylpiperidin-1-yl)propyl]}carboxamide-2,6-dimethyl-4-(4-nitrophenyl)pyridine hydrochloride (98). A mixture of
5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.63 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (181.3 mg, 0.946 mmol, 1.50 equiv) and 4-dimethylaminopyridine (84.7 mg, 0.690 mmol, 1.10 equiv) in anhydrous CH₂Cl₂ (20 mL) was stirred
20 at room temperature under argon for 1 hour. A solution of 1-(3-aminopropyl)-4-(4-methoxyphenyl)-4-phenylpiperidine (245 mg, 0.755 mmol, 1.20 equiv) in CH₂Cl₂ (10 mL) was injected, and the mixture was stirred at reflux for 6 hours. The mixture was cooled to room
25 temperature, diluted with CH₂Cl₂ (150 mL), and washed with saturated aqueous NH₄Cl (3 x 40 mL). The organic phase was dried over MgSO₄ and concentrated. The residue was purified by flash chromatography (SiO₂, CHCl₃-MeOH-methanolic ammonia (2 M) 100:4:2) to afford 275 mg (70%)
30 of 98 free base as a yellow solid, which was characterized spectroscopically. To a solution of this product in CH₂Cl₂ (10 mL) was added HCl in ether (1.0 M,

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0.8 mL, 1.8 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 225 mg of 98 hydrochloride (yellow solid): m.p. 185 °C (decomp.); Anal. Calcd. for $\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}_3 \cdot \text{HCl} \cdot 0.4 \text{ CH}_2\text{Cl}_2$: C, 62.98; H, 6.21; N, 10.09. Found: C, 63.02; H, 6.40; N, 9.76.

EXAMPLE 99

10

1-Benzyl-4-methyl-piperidin-4-ol. To a solution of 1-benzyl-4-piperidone (5.00 mL, 27.0 mmol, 1.00 equiv, Aldrich) in anhydrous ether at -78 °C under argon was added methyllithium (1.4 M in Et_2O , 54.0 mL, 53.9 mmol, 2.00 equiv). Stirring was continued at -78 °C for 1.5 hours. Ether (200 mL) and water (40 mL) were added, and the two phases were separated. The aqueous solution was extracted with Et_2O (3 x 50 mL). The combined organic solutions were dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , EtOAc to EtOAc-MeOH 9:1) to give 4.81 g (87%) of colorless oil, which was characterized spectroscopically.

1-Benzyl-4-methyl-4-phenylpiperidino. 1-Benzyl-4-methyl-piperidin-4-ol (4.81 g, 23.4 mmol, 1.00 equiv) was added to a suspension of AlCl_3 (15.62 g, 117 mmol, 5.00 equiv) in benzene (100 mL) at room temperature under argon. The mixture was stirred at reflux for 24 hours, then cooled and poured cautiously into ice water (100 g of ice plus 50 mL of water). The aqueous phase was adjusted to pH 11-12 by addition of 6 N aqueous NaOH at 0 °C, and extracted with EtOAc (3 x 100 mL). The combined organic solutions were dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , hexane- Et_2O 19:1 to 9:1 followed by hexane-EtOAc 3:1) to give 3.23 g (52%) of brown oil, which was characterized spectroscopically.

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4-Methyl-4-phenylpiperidine. Freshly prepared methanolic formic acid solution (4.4% by weight, 70 mL) was added to 1-benzyl-4-methyl-4-phenylpiperidine (3.23 g, 12.2 mmol, 1.00 equiv). To the resulting solution was added
5 palladium on carbon (10% Pd, 2.00 g). The mixture was stirred at room temperature for 24 hours. The solid was filtered out and washed with MeOH (30 mL), H₂O (15 mL), CH₂Cl₂ (30 mL) and MeOH (15 mL). The combined filtrate and washings were concentrated, and the residue was
10 dissolved in CH₂Cl₂ (50 mL) and H₂O (10 mL). The aqueous phase was adjusted to pH 11 by addition of 1 N aqueous NaOH. The organic phase was separated, dried over MgSO₄ and concentrated. The residual oil was purified by flash chromatography (SiO₂, CHCl₃-MeOH-NH₃ (2.0 M in MeOH)
15 100:4:0 to 100:20:10) to afford 1.20 g of 1-benzyl-4-methyl-4-phenylpiperidine and 1.10 g (51%, 82% based on unrecovered starting material) of 4-methyl-4-phenylpiperidine, which was characterized spectroscopically.

20

3-Aminopropyl-4-methyl-4-phenylpiperidine. 4-Methyl-4-phenylpiperidine (1.00 g, 5.70 mmol, 1.00 equiv), 3-bromopropylamine hydrobromide (1.87 g, 8.55 mmol, 1.00 equiv) and potassium carbonate (1.97 g, 14.2 mmol, 2.5
25 equiv) were stirred in refluxing dioxane (20 mL) for 36 hours. After removal of the solvent, water (50 mL) was added and the pH was adjusted to 11-12 by addition of 1 N aqueous NaOH. The mixture was extracted with CH₂Cl₂ (150 mL + 3 x 100 mL). The combined organic solutions
30 were dried over MgSO₄ and concentrated. The residue was purified by flash chromatography (SiO₂, CHCl₃-MeOH-NH₃ (2 M in MeOH) 100:20:10) to give 241 mg (18%) of colorless oil, which was characterized spectroscopically.

35 5-Carboxamide-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-methyl-4-phenylpiperidin-1-yl)propyl]}carboxamide-4-(4-nitrophenyl)pyridine hydrochloride hydrate (99). A

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mixture of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (148 mg, 0.465 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (149 mg, 0.776 mmol, 1.67 equiv) and 4-dimethylaminopyridine (69.5 mg, 0.569 mmol, 1.22 equiv) in anhydrous CH_2Cl_2 (15 mL) was stirred at room temperature under argon for 1 hour. A solution of 3-aminopropyl-4-methyl-4-phenylpiperidine (120 mg, 0.517 mmol, 1.11 equiv) in CH_2Cl_2 (5 mL) was injected, and stirring was continued at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (120 mL), and washed with saturated aqueous NH_4Cl (3 x 35 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH-methanolic ammonia (2 M) 100:3:1.5 to 100:4:2) to afford 135 mg (54%) of 99 free base as a yellow solid, which was characterized spectroscopically. To a solution of this product (132 mg, 0.25 mmol, 1.0 equiv) in CH_2Cl_2 (4 mL) and MeOH (1 mL) was added HCl in ether (1.0 M, 0.5 mL, 2.0 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (4 mL) and MeOH (1 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 110 mg of yellow solid: m.p. 178 °C (decomp.); Anal. Calcd. for $\text{C}_{30}\text{H}_{37}\text{N}_5\text{O}_4 \cdot \text{HCl} \cdot 1.4 \text{ H}_2\text{O}$: C, 60.73; H, 6.93; N, 11.80. Found: C, 60.76; H, 6.96; N, 11.70.

EXAMPLE 100

6-Ethyl-2,2-dimethyl-2H,4H-1,3-dioxin-4-one. To a solution of 2,2-dimethyl-1,3-dioxan-4,6-dione 1 (40.4 g, 280 mmol, 1.00 equiv, Aldrich) in anhydrous CH_2Cl_2 (300 mL) at 0 °C under argon was added propionyl chloride (26.7 mL, 308 mmol, 1.10 equiv) followed by pyridine (45.3 mL, 560 mmol, 2.00 equiv). The resulting mixture was stirred at 0 °C for 1 hour and then at room temperature for 5 hours. The organic solution was washed with 1 N aqueous

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HCl (2 x 100 mL) and water (3 x 100 mL), dried over MgSO_4 and concentrated to give 32 g of 2,2-dimethyl-5-propanoyl-1,3-dioxan-4,6-dione as a purple solid, which was characterized spectroscopically. A solution of this solid and acetone (10.3 mL, 140 mmol, 0.50 equiv) in toluene (300 mL) was stirred at reflux under argon for 1.5 hours. After removal of the solvents, the residue was distilled at reduced pressure to afford 15.0 g (34%) of colorless oil (b.p. 85-87 °C/0.5 mm Hg), which was characterized spectroscopically.

3-Amino-2-pentanoic acid. Anhydrous ammonia gas was passed into a solution of 6-ethyl-2,2-dimethyl-2H,4H-1,3-dioxin-4-one (15.1 g, 96.7 mmol) in p-xylene (240 mL) at 115 °C (bath temperature) for 5 hours. The mixture was cooled to room temperature, diluted with CHCl_3 (145 mL), dried over MgSO_4 , and concentrated to afford 10.05 g (91%) of light yellow oil, which was characterized spectroscopically and used for the next step without purification.

2-Cyanoethyl 3-oxopentanoate. A solution of ethyl propionylacetate (50 g, 0.35 mol, 1.0 equiv) and 3-hydroxypropionitrile (35 mL, 0.52 mol, 1.5 equiv) was heated at 190-210 °C while EtOH (19 mL) was collected by distillation. The residue was distilled in vacuo to afford 37 g (63%) of yellow oil (b.p. 120-125 °C/0.4 mm Hg), which was characterized spectroscopically.

2-Cyanoethyl 2-(4-nitrophenyl)ethyl-3-oxopentanoate. In a dry flask, a mixture of 4-nitrobenzaldehyde (12.7 g, 84.3 mmol, 1.00 equiv), 2-cyanoethyl 3-oxopentanoate (15.0 g, 88.7 mmol, 1.00 equiv), piperidine (0.44 mL, 4.4 mmol, 0.05 equiv) and acetic acid (0.25 mL, 4.4 mmol, 0.05 equiv) in 2-propanol (200 mL) was stirred at room temperature under argon for 24 hours. The resulting white precipitate was collected by filtration, washed

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with cold 2-propanol (3 x 50 mL), and dried to afford 24.6 g (96%) of white solid, which was characterized spectroscopically.

- 5 5-Carboxamide-3-(2-cyanoethoxy)carbonyl-2, 6-diethyl-1,4-dihydro-4-(4-nitrophenyl) pyridine. A mixture of 2-cyanoethyl 2-(4-nitrophenyl)methylene-3-oxopentanoate (24.2 g, 80.1 mmol, 1.00 equiv) and 3-amino-2-pentenamide (10.1 g, 88.1 mmol, 1.10 equiv) in EtOH was stirred at
- 10 reflux under argon for 14 hours. Removal of the solvent afforded 32.1 g (91% crude yield) of yellow solid, which was characterized spectroscopically and used for the next step without purification.
- 15 5-Carboxamide-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid. Aqueous NaOH (1 N, 204 mL, 204 mmol, 3.0 equiv) was added slowly with stirring at -5 °C to a solution of 5-carboxamido-3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)
- 20 pyridine (27.1 g, 68.0 mmol, 1.0 equiv) in acetone (100 mL) and stirring was continued at -5 - 0 °C for 1 hour. Acetone was removed in vacuo at 10 °C. The aqueous solution was extracted with EtOAc (2 x 150 mL) and CH₂Cl₂ (2 x 100 mL), and the organic extracts were discarded.
- 25 The aqueous phase was acidified to pH 2-3 by addition of 6 N aqueous HCl (ca. 340 mL) with stirring at -5 - 0 °C, and stirring was continued for 30 minutes at 0 °C. The resulting solid was collected by filtration, washed with water (2 x 30 mL), and dried in vacuo at room temperature
- 30 to give 22.1 g (94%) of yellow solid, which was characterized spectroscopically.

- 5-Carboxamide-2,6-diethyl-1,4-dihydro-3-{N-[3-(4-hydroxy-4-phenylpiperidin-1-yl)propyl]}carboxamide-4-(4-
- 35 nitrophenyl)pyridine hydrochloride hydrate (100). A mixture of 5-carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (250 mg, 0.724

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mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (208.2 mg, 1.086 mmol, 1.50 equiv) and 4-dimethylaminopyridine (92.3 mg, 0.796 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (15 mL) was stirred at room temperature under argon for 1 hour. A solution of 1-(3-aminopropyl)-4-hydroxy-4-phenylpiperidine (203.6 mg, 0.870 mmol, 1.20 equiv) in CH_2Cl_2 (10 mL) was injected, and the mixture was stirred at reflux for 14 hours. Anhydrous DMF (8 mL) was injected, and the resulting clear solution was refluxed for an additional hour. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (150 mL), and washed with saturated aqueous NH_4Cl (3 x 40 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH-methanolic ammonia (2 M) 100:8:6) to afford 188 mg (46%) of 100 free base as a yellow solid, which was characterized spectroscopically. To a solution of this product in CH_2Cl_2 (10 mL) was added HCl in ether (1.0 M, 0.6 mL, 1.8 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 202 mg of 100 hydrochloride hydrate (yellow solid): m.p. 165 °C (decomp.); Anal. Calcd. for $\text{C}_{31}\text{H}_{39}\text{N}_5\text{O}_5 \cdot \text{HCl} \cdot 1.8 \text{ H}_2\text{O}$: C, 59.05; H, 6.97; N, 11.11. Found: C, 58.98; H, 6.70; N, 11.09.

EXAMPLE 101

3-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]propionitrile. Acrylonitrile (2.33 mL, 35.4 mmol, 2.50 equiv) was added at 0 °C to a solution of 4-(4-chlorophenyl)-4-hydroxypiperidine (3.00 g, 14.2 mmol, 1.00 equiv, Aldrich) in EtOH (30 mL) and the resulting solution was stirred for 1.5 hours at room temperature. The solvent was removed to give 3.71 g (99%) of white solid, which was characterized spectroscopically and used

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without purification for the next reaction.

1-(3-aminopropyl)-4-(4-chlorophenyl)-4-hydroxypiperidine.
To a stirred solution of 3-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]propionitrile (3.51 g, 13.2 mmol, 1.0 equiv) in anhydrous THF (20 mL) under argon was added a solution of BH_3 in THF (1.0 M, 46.4 mL, 3.5 equiv) at room temperature. The mixture was refluxed for 4.5 hours and then cooled to room temperature. Aqueous HCl (6 N, 30 mL) was added and stirring was continued for 2 hours at 55-60 °C. The mixture was basified to pH 9 by addition of 6 N aqueous NaOH and extracted with CH_2Cl_2 (3 x 150 mL). The combined organic solutions were dried over MgSO_4 and concentrated. The residue was dissolved in CH_2Cl_2 (20 mL) and treated with HCl in ether (1.0 M, 27.7 mL, 2.1 equiv). The solvents were removed, ether (60 mL) was added, the mixture was filtered, and the filter cake was washed with ether (2 x 20 mL). Water (40 mL) was added to the resulting white solid, the pH was adjusted to 10 with 1 M NaOH, and the aqueous phase was extracted with CH_2Cl_2 (3 x 80 mL). The combined organic solutions were dried over MgSO_4 and concentrated to give 3.10 g (87%) of white solid, which was characterized spectroscopically.

25

5-Carboxamido-2,6-diethyl-1,4-dihydro-3-{N-[3-(4-hydroxy-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine hydrochloride hydrate (101). A mixture of 5-carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (250 mg, 0.724 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (208.2 mg, 1.086 mmol, 1.50 equiv) and 4-dimethylaminopyridine (92.3 mg, 0.796 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (15 mL) was stirred at room temperature under argon for 1 hour. A solution of 1-(3-aminopropyl)-4-chlorophenyl-4-hydroxypiperidine (233.5 mg, 0.870 mmol, 1.20 equiv) in CH_2Cl_2 (10 mL) was

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injected, and the mixture was stirred at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (150 mL), and washed with saturated aqueous NH_4Cl (3 x 40 mL). The organic phase was dried
 5 over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH-methanolic ammonia (2 M) 90:8:5) to afford 256 mg (59%) of 101 free base as a yellow solid, which was characterized spectroscopically. To a solution of this product in CH_2Cl_2 (10
 10 mL) was added HCl in ether (1.0 M, 0.8 mL, 1.9 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 224 mg of yellow solid: m.p. 164 °C (decomp.); Anal. Calcd. for
 15 $\text{C}_{27}\text{H}_{32}\text{N}_4\text{O}_5 \cdot \text{HCl} \cdot 1.8 \text{ H}_2\text{O}$: C, 59.05; H, 6.97; N, 11.11. Found: C, 58.98; H, 6.70; N, 11.09.

EXAMPLE 102

20 5-Carboxanide-3-{N-[(4-cyano-4-phenylpiperidin-1-yl)propyl]}carboxanide-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine hydrochloride hydrate (102). A mixture of 5-carboxanide-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (1.00 g, 2.90
 25 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (830 mg, 4.34 mmol, 1.50 equiv) and 4-dimethylaminopyridine (389.7 mg, 3.19 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (50 mL) was stirred at room temperature under argon for 1 hour. A solution of
 30 1-(3-aminopropyl)-4-cyano-4-phenylpiperidine (848 mg, 3.48 mmol, 1.20 equiv) in CH_2Cl_2 (10 mL) was injected, and the mixture was stirred at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (250 mL), and washed with saturated aqueous NH_4Cl
 35 (3 x 80 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH-methanolic ammonia (2 M)

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100:2:1 to 100:3:1.5) to afford 1.53 g (92%) of yellow solid (102), which was characterized spectroscopically. To a solution of this product (1.51 g, 2.65 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) was added a solution of HCl in ether (1.0 M, 5.2 mL, 2.0 equiv) at room temperature. After removal of the solvents, a solution of the residue in CH_2Cl_2 (10 mL) was added dropwise with swirling to ether (50 mL). The resulting precipitate was collected by filtration and dried *in vacuo* at 85 °C to afford 1.47 g of yellow powder: m.p. 210 °C; Anal. Calcd. for $\text{C}_{32}\text{H}_{38}\text{N}_6\text{O}_4 \cdot \text{HCl} \cdot 1.2 \text{ H}_2\text{O}$: C, 61.13; H, 6.64; N, 13.37. Found: C, 61.02; H, 6.44; N, 13.12.

(-)- and (+)-102 hydrochloride hydrate. The enantiomers of 102 free base (500 mg) were separated in four injections on a Chiralpak AS column (20 x 250 mm, Daicel), which was eluted with EtOH-hexane 15:85 at 9.0 mL/min with UV detection at 300 nm. The first major peak eluted at 43 min. To a solution of this product ($[\alpha]_D = +13.1^\circ$ (EtOH, 0.0233 g/mL)) in EtOH (10 mL) was added HCl in ether (1.0 M, 0.36 mL) at 0 °C. After removal of the solvents, a solution of the residue in EtOH (2 mL) was added dropwise into ether (50 mL) with swirling to give, after filtration, 153.6 mg of yellow powder: $[\alpha]_D = -36.6^\circ$ (EtOH, 0.00975 g/mL); m.p. 230 °C (decomp.); Anal. Calcd. for $\text{C}_{32}\text{H}_{38}\text{N}_6\text{O}_4 \cdot \text{HCl} \cdot 1.57 \text{ H}_2\text{O}$: C, 60.49; H, 6.68; N, 13.23. Found: C, 60.19; H, 6.28; N, 13.01. The second major component eluted at 71 min ($[\alpha]_D = -17.4^\circ$ (EtOH, 0.03155 g/mL)). This product was converted to the HCl salt and precipitated as described for the other enantiomer to afford 168.6 mg of yellow powder: $[\alpha]_D = +28.6^\circ$ (EtOH, 0.0101 g/mL); m.p. 230 °C (decomp.); Anal. Calcd. for $\text{C}_{32}\text{H}_{38}\text{N}_6\text{O}_4 \cdot \text{HCl} \cdot 1.57 \text{ H}_2\text{O}$: C, 60.49; H, 6.68; N, 13.23. Found: C, 60.25; H, 6.34; N, 12.92.

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EXAMPLE 103

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4,4-bis-(4-Methoxyphenyl)piperidino. To a solution of AlCl_3 (26.0 g, 0.195 mmol, 6.00 equiv) in anhydrous anisole (100 mL) at 0 °C under argon was added 4-piperidone hydrate hydrochloride (5.00 g, 32.5 mmol, 1.00 equiv). Stirring was continued at 0 °C for 3 hours and then at room temperature for 12 hours. The mixture was added cautiously to ice water (100 g of ice plus 50 mL of water). The aqueous phase was extracted with Et_2O (3 x 50 mL) and the combined organic solutions were concentrated. The resulting white solid was dissolved in water (100 mL). This solution was basified to pH 11-12 by addition of 1N aqueous NaOH, and extracted with CH_2Cl_2 (250 mL + 3 x 150 mL). The combined organic solutions were dried over MgSO_4 and concentrated to afford 9.38 g (97%) of colorless oil, which was characterized spectroscopically.

1-(3-Aminopropyl)-4,4-bis-(4-Methoxyphenyl)piperidino. 4,4-bis-(4-Methoxyphenyl)piperidine (9.01 g, 30.3 mmol, 1.00 equiv), 3-bromopropylamine hydrobromide (6.66 g, 30.3 mmol, 1.00 equiv) and potassium carbonate (5.02 g, 36.3 mmol, 1.20 equiv) were stirred in refluxing anhydrous 1,4-dioxane (200 mL) for 12 hours. After removal of dioxane, water (200 mL) was added and the pH was adjusted to 11-12 by addition of 1 N aqueous NaOH. The mixture was extracted with CH_2Cl_2 (4 x 200 mL). The combined organic solutions were dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH- NH_3 (2 M in MeOH) 100:20:10) to give 6.50 g of 4,4-bis-(4-methoxyphenyl)piperidine and 2.70 g (25%, 90% after correction for recovered starting material) of 1-(3-aminopropyl)-4,4-bis-(4-methoxyphenyl)piperidine (colorless oil), which was characterized spectroscopically.

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5-Carboxanido-2,6-diethyl-1,4-dihydro-3-{N-[3-(4,4-bis-(4-methoxyphenyl)piperidin-1-yl)propyl]}carboxanido}-4-

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(4-nitrophenyl)pyridine hydrochloride (103). A mixture of 5-carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (300 mg, 0.869 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (250.0 mg, 1.30 mmol, 1.50 equiv) and 4-dimethylaminopyridine (116.9 mg, 0.957 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (18 mL) was stirred at room temperature under argon for 1 hour. A solution of 1-(3-aminopropyl)-4,4-bis-(4-methoxyphenyl)piperidine (369.6 mg, 1.04 mmol, 1.20 equiv) in CH_2Cl_2 (12 mL) was injected, and the mixture was stirred at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (180 mL), and washed with saturated aqueous NH_4Cl (3 x 50 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH-methanolic ammonia (2 M) 100:4:2 to 100:5:2.5) to afford 535 mg (90%) of 103 free base as a yellow solid, which was characterized spectroscopically. To a solution of this product (520 mg, 0.760 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) was added HCl in ether (1.0 M, 1.5 mL, 2.0 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (8 mL) and added dropwise to ether (50 mL) with swirling to give, after filtration, 465 mg of yellow solid: m.p. 175 °C (decomp.); Anal. Calcd. for $\text{C}_{29}\text{H}_{40}\text{N}_6\text{O}_6 \cdot \text{HCl} \cdot 1.5 \text{ H}_2\text{O}$: C, 62.85; H, 6.90; N, 9.40. Found: C, 62.95; H, 6.80; N, 9.16.

EXAMPLE 104

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1-(3-Aminopropyl)-4-phenylpiperazine. 4-Phenylpiperazine (5.00 g, 30.8 mmol, 1.00 equiv, Aldrich), 3-bromopropylamine hydrobromide (8.09 g, 37.0 mmol, 1.20 equiv) and potassium carbonate (8.51 g, 61.6 mmol, 2.00 equiv) were stirred in refluxing acetone (200 mL) and EtOH (40 mL) for 14 hours. After removal of the solvents, water (250 mL) was added and the pH was

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adjusted to 11-12 by addition of 1 N aqueous NaOH. The mixture was extracted with CH_2Cl_2 (4 x 250 mL). The combined organic solutions were dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH- NH_3 (2 M in MeOH) 100:10:5 to 100:20:10) to give 3.80 g (56%) of yellow oil, which was characterized spectroscopically.

5-Carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4-phenylpiperazin-1-yl)propyl]}carboxamide-pyridine hydrochloride hydrate (104). A mixture of 5-carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (250 mg, 0.724 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (208 mg, 1.09 mmol, 1.50 equiv) and 4-dimethylaminopyridine (97.2 mg, 0.796 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (15 mL) was stirred at room temperature under argon for 1 hour. A solution of 1-(3-aminopropyl)-4-phenylpiperazine (190 mg, 0.869 mmol, 1.20 equiv) in CH_2Cl_2 (10 mL) was injected, and stirring was continued at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (150 mL), and washed with saturated aqueous NH_4Cl (3 x 40 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH-methanolic ammonia (2 M) 100:4:2) to afford 317 mg (80%) of 104 free base as a yellow solid, which was characterized spectroscopically. To a solution of this product (302 mg, 0.550 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) was added HCl in ether (1.0 M, 1.5 mL, 2.7 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 285 mg of yellow solid: m.p. 160 °C (decomp.); Anal. Calcd. for $\text{C}_{29}\text{H}_{39}\text{N}_6\text{O}_4 \cdot \text{HCl} \cdot 1.2 \text{ H}_2\text{O}$: C, 59.58; H, 6.90; N, 13.86. Found: C, 59.49; H, 6.74; N, 13.67.

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EXAMPLE 105

8-(3-Aminopropyl)-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one. 1-Phenyl-1,3,8-triazaspiro[4.5]decan-4-one (5.00 g, 21.6 mmol, 1.00 equiv), 3-bromopropylamine hydrobromide (4.73 g, 21.6 mmol, 1.00 equiv) and potassium carbonate (2.99 g, 21.6 mmol, 1.00 equiv) were stirred in refluxing dioxane (70 mL) for 24 hours. After removal of the solvent, water (50 mL) was added and the pH was adjusted to 11-12 by addition of 1 N aqueous NaOH. The mixture was extracted with CH₂Cl₂ (200 mL + 3 x 100 mL). The combined organic solutions were dried over MgSO₄ and concentrated. The residue was purified by flash chromatography (SiO₂, CHCl₃-MeOH-NH₃ (2 M in MeOH) 100:20:10 to 100:24:12) to give 250 mg (4%) of white solid, which was characterized spectroscopically.

5-Carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[(3-(1-phenyl-4-oxo-1,3,8-triazaspiro[4.5]decan-8-yl)propyl)]carbamidopyridino hydrochloride hydrate (105). A mixture of 5-carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.580 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (166 mg, 0.869 mmol, 1.50 equiv) and 4-dimethylaminopyridine (77.9 mg, 0.638 mmol, 1.10 equiv) in anhydrous CH₂Cl₂ (15 mL) was stirred at room temperature under argon for 1 hour. A solution of 8-(3-aminopropyl)-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one (200.7 mg, 0.696 mmol, 1.20 equiv) in CH₂Cl₂ (10 mL) was injected, and stirring was continued at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH₂Cl₂ (150 mL), and washed with saturated aqueous NH₄Cl (3 x 40 mL). The organic phase was dried over MgSO₄ and concentrated. The residue was purified by flash chromatography (SiO₂, CHCl₃-MeOH-methanolic ammonia (2 M) 100:2:1 to 100:4:2) to afford 230 mg (65%) of 105 free base as a yellow solid, which was characterized

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spectroscopically. To a solution of this product (215, 0.349 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) and MeOH (1 mL) was added HCl in ether (1.0 M, 0.8 mL, 2.3 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and MeOH (1 mL) and added dropwise to ether (30 mL) with swirling to give, after filtration, 165 mg of yellow solid: m.p. 187 °C (decomp.); Anal. Calcd. for $\text{C}_{33}\text{H}_{41}\text{N}_7\text{O}_5 \cdot \text{HCl} \cdot 1.4 \text{ H}_2\text{O}$: C, 58.51; H, 6.67; N, 14.47. Found: C, 58.73; H, 6.80; N, 14.32.

10

EXAMPLE 106

5-Carboxamido-2,6-diethyl-1,4-dihydro-3-{N-[3-(4-methyl-4-phenyl piperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine hydrochloride hydrate (106). A mixture of 5-carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (160 mg, 0.465 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (149 mg, 0.776 mmol, 1.67 equiv) and 4-dimethylaminopyridine (69.5 mg, 0.569 mmol, 1.22 equiv) in anhydrous CH_2Cl_2 (15 mL) was stirred at room temperature under argon for 1 hour. A solution of 3-aminopropyl-4-methyl-4-phenylpiperidine (120 mg, 0.517 mmol, 1.11 equiv) in CH_2Cl_2 (5 mL) was injected, and stirring was continued at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (120 mL), and washed with saturated aqueous NH_4Cl (3 x 35 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH-methanolic ammonia (2 M) 100:3:1.5 to 100:4:2) to afford 185 mg (71%) of 106 free base as a yellow solid, which was characterized spectroscopically. To a solution of this product (171 mg, 0.306 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) and MeOH (1 mL) was added HCl in ether (1.0 M, 0.7 mL, 2.3 equiv). After removal of the solvents, the residue was dissolved in CH_2Cl_2 (5 mL) and MeOH (1 mL) and added dropwise to

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ether (30 mL) with swirling to give, after filtration, 155 mg of yellow solid: m.p. 166 °C (decomp.); Anal. Calcd. for $C_{12}H_{14}N_5O_4 \cdot HCl \cdot 1.2 H_2O$: C, 62.21; H, 7.24; N, 11.34. Found: C, 62.21; H, 7.46; N, 11.26.

5

EXAMPLE 107

Benzylpropionylacetate. A mixture of ethylpropionyl acetate (50.0 g, 0.347 mol, 1.00 equiv) and benzyl
10 alcohol (39.5 mL, 0.381 mol, 1.10 equiv) was stirred at 180-210 °C for ca. 3 hours while EtOH was collected by distillation (ca. 20 mL of EtOH was collected). The product was distilled (b.p. 115-120 °C/0.4 mm Hg) to afford 54.8 g (76%) of colorless oil, which was
15 characterized spectroscopically.

Benzyl 3-amino-2-pentenoate. A mixture of benzylpropionylacetate (54.80 g, 265.7 mmol) and molecular sieves (14 g, 3A, Mallinckrodt) was stirred at
20 50 °C for 40 hours while NH_3 gas was bubbled through the solution. The product was decanted to give 55.5 g of colorless oil, which was characterized spectroscopically and used for the next reaction without purification.

25 **3-Benzylloxycarbonyl-5-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitro)phenylpyridine.** A mixture of 2-cyanoethyl 2-(4-nitrophenyl)methylene-3-oxopentanoate (9.80 g, 32.4 mmol, 1.00 equiv) and benzyl 3-amino-2-pentenoate (7.99 g, 38.9 mmol, 1.20 equiv) in
30 EtOH (150 mL) was stirred at reflux for 36 hours. The solvent was removed to give 15.4 g (97%) of yellow solid, which was characterized spectroscopically and used for the next reaction without purification.

35 **3-(2-Cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-5-carboxylic acid.** A solution of 3-benzylloxycarbonyl-5-(2-cyanoethoxy)carbonyl-2,6-diethyl-

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1,4-dihydro-4-(4-nitro)phenylpyridine (3.84 g, 7.84 mmol) in methanolic formic acid solution (4.4% by weight, 10 mL) was added to a suspension of Pd on carbon (10%, 3.84 g) in methanolic formic acid solution (4.4% by weight, 90 mL). The mixture was stirred for 20 minutes, then filtered through Celite. After removal of the solvents, a solution of the residue in CH_2Cl_2 (150 mL) was washed with 0.1 N aqueous HCl (15 mL) and water (15 mL), dried over MgSO_4 and concentrated to give 2.95 g (94%) of yellow solid, which was characterized spectroscopically and used for subsequent reactions without purification.

5-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-5-(N-methyl)carboxamide-4-(4-nitro)phenylpyridine. A mixture of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-5-carboxylic acid (3.70 g, 9.26 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.66 g, 13.9 mmol, 1.50 equiv) and 4-dimethylaminopyridine (1.24 g, 10.2 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (200 mL) was stirred at room temperature under argon for 1 hour. Aqueous methylamine (40% by weight, 1.60 mL, 18.5 mmol, 2.00 equiv) was injected, and stirring was continued for 20 hours. The resulting solution was washed with 0.1 N HCl (3 x 50 mL), dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH 100:2) to afford 3.51 g (92%) of yellow solid, which was characterized spectroscopically.

2,6-Diethyl-1,4-dihydro-5-(N-methyl)carboxamide-4-nitrophenylpyridine-3-carboxylic acid. To a solution of 5-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-5-(N-methyl)carboxamide-4-(4-nitro)phenylpyridine (3.25 g, 7.88 mmol, 1.00 equiv) in acetone (32 mL) was added 1 N aqueous NaOH (23.6 mL, 23.6 mmol, 3.00 equiv) at -5-0 °C. The mixture was stirred for 3 hours at this temperature. After removal of acetone *in vacuo* at 10 °C, the mixture was

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extracted with EtOAc (15 mL). The aqueous solution was cooled to 0 °C and adjusted to pH 3-4 by addition of 6 N aqueous HCl. The resulting precipitate was collected by filtration, washed with water (20 mL) and dried to afford
5 2.51 g (89%) of yellow solid, which was characterized spectroscopically.

2,6-Diethyl-1,4-dihydro-3-{N-[3-(4-(4-methoxyphenyl)-4-phenylpiperidin-1-yl)propyl]}carboxamido-5-N-methylcarboxamido-4-(4-nitrophenyl)pyridine (107). A mixture of
10 2,6-diethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.558 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (160 mg, 0.837 mmol, 1.50
15 equiv) and 4-dimethylaminopyridine (75.0 mg, 0.614 mmol, 1.10 equiv) in anhydrous CH₂Cl₂ (15 mL) was stirred at room temperature under argon for 1 hour. A solution of 3-aminopropyl-4-(4-methoxyphenyl)-4-phenylpiperidine (217
20 mg, 0.670 mmol, 1.20 equiv) in CH₂Cl₂ (5 mL) was injected, and stirring was continued at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH₂Cl₂ (150 mL), and washed with saturated aqueous NH₄Cl (3 x 40 mL). The organic phase was dried over MgSO₄ and concentrated. The residue was purified by flash
25 chromatography (SiO₂, CHCl₃-MeOH-methanolic ammonia (2 M) 100:4:2) to afford 258 mg (69%) of yellow solid: m.p. 133 °C (decomp.); Anal. Calcd. for C₃₉H₄₇N₅O₅·0.25 CHCl₃: C, 67.77; H, 6.85; N, 10.07. Found: C, 67.56; H, 7.04; N, 10.16.

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EXAMPLE 108

3-(4-Methoxy-4-phenyl)piperidin-1-ylpropionitrile. In a dry flask under argon, sodium hydride (60% dispersion in
35 mineral oil, 520 mg, 13 mmol, 3.0 equiv) was washed with three times with hexane, and the washings were discarded. The reaction flask was cooled to 0 °C, a solution of 3-

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(4-hydroxy-4-phenyl)piperidin-1-ylpropionitrile (1.0 g, 4.3 mmol, 1.0 equiv) in anhydrous THF (20 mL) was added, and the mixture was stirred for 30 minutes. Iodomethane (0.40 mL, 6.5 mmol, 1.5 equiv) was added, and stirring
5 was continued at 0 °C for 1 hour and at room temperature for 2 hours. Ethyl acetate (30 mL) and water (20 mL) were added cautiously. The aqueous phase was basified to pH 10-11 by addition of 1 N aqueous NaOH and extracted with EtOAc (2 x 100 mL) and CH₂Cl₂ (2 x 100 mL). The
10 combined organic solutions were dried over MgSO₄ and concentrated. The residue was purified by flash chromatography (SiO₂, hexane-EtOAc 2:1 to 1:1) to give 542 mg (51%) of white solid, which was characterized spectroscopically.

15

1-(3-Aminopropyl)-4-methoxy-4-phenylpiperidine. Borane-tetrahydrofuran complex (1.0 M in THF, 7.4 mL, 7.4 mmol, 3.5 equiv) was added under argon to neat 3-(4-methoxy-4-phenyl)piperidin-1-ylpropionitrile (512 mg, 2.10 mmol, 1.0 equiv). The mixture was stirred at reflux for 5
20 hours and then cooled to 0 °C. Aqueous HCl (6 N, 8 mL) was added cautiously, and stirring was continued at room temperature overnight, then at 42 °C for 1.5 hours. The solution was basified to pH 10-11 by addition of 6 N
25 aqueous NaOH and extracted with CH₂Cl₂ (3 x 60 mL). The combined organic solutions were dried over MgSO₄ and concentrated. The residue was purified by flash chromatography (SiO₂, CHCl₃-MeOH-NH₃ (2.0 M in MeOH) to give 387 mg (75%) of colorless oil, which was
30 characterized spectroscopically.

2,6-Diethyl-1,4-dihydro-3-{N-[3-(4-methoxy-4-phenylpiperidin-1-yl)propyl]carboxamide}-5-(N-methyl)carboxamide-4-(4-nitrophenyl)pyridine (108). A mixture of 2,6-
35 diethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.558 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-

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ethylcarbodiimide hydrochloride (160 mg, 0.837 mmol, 1.50 equiv) and 4-dimethylaminopyridine (75.0 mg, 0.614 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (15 mL) was stirred at room temperature under argon for 1 hour. A solution of
5 3-aminopropyl-4-methoxy-4-phenylpiperidine (166 mg, 0.670 mmol, 1.20 equiv) in CH_2Cl_2 (5 mL) was injected, and stirring was continued at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (150 mL), and washed with saturated aqueous NH_4Cl
10 (3 x 40 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH- NH_3 (2 M in MeOH) 100:3:1.5 to 100:4:2) to afford 230 mg (70%) of yellow solid: m.p. 240 °C (decomp.); Anal. Calcd. for
15 $\text{C}_{33}\text{H}_{40}\text{N}_5\text{O}_5 \cdot 0.2 \text{CHCl}_3$: C, 64.99; H, 7.10; N, 11.41. Found: C, 64.94; H, 7.36; N, 11.26.

EXAMPLE 109

20 Diphenyl-4-piperidylmethane hydrochloride. To a solution of diphenyl-4-pyridylmethane (2.00 g, 8.15 mmol, 1.00 equiv, Aldrich) in EtOH was added Rh on carbon (5%, 0.800 g). The suspension was stirred in a bomb under H_2 pressure (2.7 atm) at 55-60 °C for 7 hours. The catalyst
25 was filtered out (Celite) and washed thoroughly with CH_2Cl_2 and MeOH. The combined filtrate and washings were concentrated. The residue was dissolved in CH_2Cl_2 (5 mL) and treated with HCl in Et_2O (1.0 M, 10 mL). The solvents were removed and the residue was recrystallized from
30 EtOAc-MeOH 1:2 to afford 0.96 g of white solid. This solid was added to water (30 mL), which was adjusted to pH 11 by addition of 1 N aqueous NaOH, and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic solutions were dried over MgSO_4 and concentrated to give 0.81 g (39%) of
35 white solid, which was characterized spectroscopically.

3-(4-Diphenylmethylpiperidin-1-yl)propionitrile. To a

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solution of diphenyl-4-piperidylmethane (810 mg, 3.22 mmol, 1.00 equiv) in EtOH (5 mL) was added acrylonitrile (0.53 mL, 8.06 mmol, 2.50 equiv) dropwise at 0 °C. The mixture was stirred at room temperature for 1.5 hours and then concentrated. The residue was purified by flash chromatography (SiO₂, EtOAc-hexane 9:1 to 2:1) to give 480 mg (49%) of white solid, which was characterized spectroscopically.

10 1-(3-Aminopropyl)-4-diphenylmethyloxy-piperidine. Borane-tetrahydrofuran complex (1.0 M in THF, 5.5 mL, 5.5 mmol, 3.5 equiv) was added under argon to neat 3-(4-diphenylmethyloxy-piperidin-1-yl)propionitrile (480 mg, 1.58 mmol, 1.00 equiv). The mixture was stirred at reflux for 15 5 hours and then cooled to 0 °C. Aqueous HCl (6 N, 6 mL) was added cautiously, and stirring was continued at room temperature overnight, then at 42 °C for 1.5 hours. The solution was basified to pH 10-11 by addition of 6 N aqueous NaOH and extracted with CH₂Cl₂ (3 x 50 mL). The 20 combined organic solutions were dried over MgSO₄ and concentrated. The residue was purified by flash chromatography (SiO₂, CHCl₃-MeOH-NH₃ (2.0 M in MeOH) to give 420 mg (86%) of colorless oil, which was characterized spectroscopically.

25 2,6-Diethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophonyl)-3-{N-[3-(4-diphenylmethyloxy-piperidin-1-yl)propyl]}carboxamidopyridine (109). A mixture of 2,6-diethyl-1,4-dihydro-5-N-methylcarboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.558 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (160 mg, 0.837 mmol, 1.50 equiv) and 4-dimethylaminopyridine (75.0 mg, 0.614 mmol, 1.10 equiv) in anhydrous CH₂Cl₂ (15 mL) was stirred at 30 room temperature under argon for 1 hour. A solution of 1-(3-aminopropyl)-4-diphenylmethyloxy-piperidine (206 mg, 0.670 mmol, 1.20 equiv) in CH₂Cl₂ (5 mL) was injected, and 35

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stirring was continued at reflux for 6 hours. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (150 mL), and washed with saturated aqueous NH_4Cl (3 x 40 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 - MeOH - NH_3 (2 M in MeOH) 100:3:1.5 to 100:4:2) to afford 260 mg (72%) of yellow solid: m.p. 128 °C (decomp.); Anal. Calcd. for $\text{C}_{30}\text{H}_{47}\text{N}_5\text{O}_4 \cdot 0.30 \text{ CHCl}_3$: C, 68.85; H, 6.95; N, 10.21 Found: C, 68.78; H, 7.13; N, 10.23.

EXAMPLE 110

3-Aminopropyl-4-carboxamido-4-phenylpiperidine. 4-Carboxamido-4-phenylpiperidine (700 mg, 3.43 mmol, 1.00 equiv), 3-bromopropylamine hydrobromide (900 mg, 4.11 mmol, 1.20 equiv) and potassium carbonate (1.03 g, 7.45 mmol, 2.17 equiv) were stirred in refluxing dioxane (25 mL) for 24 hours. After removal of the solvent, the residue was purified by flash chromatography (SiO_2 , CHCl_3 - MeOH - NH_3 (2 M in MeOH) 100:8:4 to 100:20:8) to give 135 mg (14%) of colorless oil, which was characterized spectroscopically.

3-{N-[3-(4-Carboxamido-4-phenylpiperidin-1-yl)propyl]}carboxamido-2,6-diethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (110). A mixture of 2,6-diethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (126 mg, 0.352 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (102 mg, 0.530 mmol, 1.51 equiv) and 4-dimethylaminopyridine (48.0 mg, 0.393 mmol, 1.12 equiv) in anhydrous CH_2Cl_2 (7 mL) was stirred at room temperature under argon for 1 hour. A solution of 1-(3-aminopropyl)-4-carboxamido-4-phenylpiperidine (92.0 mg, 0.352 mmol, 1.00 equiv) in CH_2Cl_2 (3 mL) was injected, and stirring was continued at reflux for 6 hours. The

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mixture was cooled to room temperature, diluted with CH_2Cl_2 (100 mL), and washed with saturated aqueous NH_4Cl (3 x 30 mL). The organic phase was dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH- NH_3 (2 M in MeOH) 100:6:3 to 100:8:4) to afford 81 mg (38%) of yellow solid: m.p. 124 °C (decomp.); Anal. Calcd. for $\text{C}_{33}\text{H}_{42}\text{N}_6\text{O}_5 \cdot 0.35 \text{CHCl}_3$: C, 62.15; H, 6.62; N, 13.04 Found: C, 61.90; H, 7.00; N, 12.96.

10

EXAMPLE 111

3-(2-Cyanoethoxy)carbonyl-2,6-diethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)pyridine. A mixture of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-5-carboxylic acid (2.50 g, 6.26 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.80 g, 9.38 mmol, 1.50 equiv) and 4-dimethylaminopyridine (0.841 g, 6.89 mmol, 1.10 equiv) in anhydrous CH_2Cl_2 (50 mL) was stirred at room temperature under argon for 1.5 hours. Aqueous ethylamine (70% by weight, 2.00 mL, 31.0 mmol, 4.95 equiv) was injected, and the mixture was stirred at reflux for 5 hours and then at room temperature for 12 hours. The resulting solution was washed with saturated aqueous NH_3 (3 x 50 mL), dried over MgSO_4 and concentrated. The residue was purified by flash chromatography (SiO_2 , CHCl_3 -MeOH- NH_3 (2.0 M in MeOH) 90:8:4) to afford 2.11 g (79%) of yellow solid, which was characterized spectroscopically.

2,6-Diethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid. To a solution of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)pyridine (2.11 g, 4.95 mmol, 1.00 equiv) in acetone (20 mL) was added 1 N aqueous NaOH (14.8 mL, 14.8 mmol, 3.00 equiv) at -5-0 °C.

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The mixture was stirred for 30 minutes at this temperature. After removal of acetone in vacuo at 10 °C, the aqueous solution was cooled to 0 °C and adjusted to pH 3-4 by addition of 6 N aqueous HCl. The resulting
 5 precipitate was collected by filtration, washed with water (20 mL) and dried to afford 1.09 g (59%) of yellow solid, which was characterized spectroscopically.

2,6-Diethyl-5-(N-ethyl)carboxamido-1,4-dihydro-3-{N-[3-
 10 (4-(4-methoxy)phenyl)-4-phenylpiperidin-1-yl]propyl}carboxamide-4-(4-nitrophenyl)pyridine (111). A mixture of 2,6-diethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.536 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-
 15 ethylcarbodiimide hydrochloride (154 mg, 0.803 mmol, 1.50 equiv) and 4-dimethylaminopyridine (72.0 mg, 0.590 mmol, 1.10 equiv) in anhydrous CH₂Cl₂ (5 mL) was stirred at room temperature under argon for 1.5 hours. A solution of 1-(3-aminopropyl)-4-(4-methoxyphenyl)-4-phenylpiperidine
 20 (208.7 mg, 0.643 mmol, 1.20 equiv) in CH₂Cl₂ (1 mL) was injected, and stirring was continued at reflux for 5 hours. The mixture was cooled to room temperature, diluted with CH₂Cl₂ (150 mL), and washed with saturated aqueous NH₄Cl (3 x 50 mL). The organic phase was dried
 25 over MgSO₄ and concentrated. The residue was purified by flash chromatography (SiO₂, CHCl₃-MeOH-NH₃ (2 M in MeOH) 90:8:4) to afford 220 mg (60%) of yellow solid: m.p. 172 °C (decomp.); Anal. Calcd. for C₄₀H₄₉N₅O₅·0.8 CHCl₃: C, 63.20; H, 6.47; N, 9.03 Found: C, 63.23; H, 6.22; N, 9.11.

EXAMPLE 112

2,6-Diethyl-1,4-dihydro-4-(3-methoxyphenyl)-3,5-bis(N-(3-
 35 (4,4-diphenylpiperidin-1-yl)propyl)carboxamide)-pyridine (112). A mixture of 2-cyanoethyl propionylacetate (1.00 g, 5.91 mmol), m-anisaldehyde (1.0 mL, d 1.119, 8.22

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- mmol) and 3-aminocrotonamide (0.89 g, 8.89 mmol) in EtOH (9 ml) was heated at reflux overnight. Then the solvent was evaporated to give an oily residue which was suspended in chloroform and flash chromatographed over silica gel (100 g). Elution with EtOAc/Hexane (1:2, 1:1 and 3:1) gave a yellow oil (336 mg). It was dissolved in EtOH (1.5 ml) and treated with NaOH (74 mg, 1.85 mmol) in water (1 ml). The solution was stirred at room temperature overnight and then washed twice with CH₂Cl₂.
- 10 Acidification of the basic layer with 5% HCl gave a precipitate which was filtered off and washed with water and EtOAc to afford an off-white solid (118 mg, 6% yield).
- 15 This solid (114 mg, 0.34 mmol) was mixed with 1-(3-dimethyl-aminopropyl)-3-ethyl-carbodiimide hydrochloride (71 mg, 0.37 mmol), 3-(4,4-diphenylpiperidin-1-yl)propylamine (108 mg, 0.37 mmol) and 4-dimethyl-aminopyridine (catalytic amount) in dry CH₂Cl₂ (5 ml).
- 20 The mixture was stirred at room temperature overnight and then concentrated. The residue was dissolved in chloroform and flash chromatographed over silica gel (16 g) eluting with EtOAc/MeOH/Et₃N (20:1:1) to give a colorless oil (72 mg, 44% yield). It was recrystallized
- 25 from EtOAc/Hexane to afford a white solid (31 mg): mp 166-170°C. Anal. Calcd. for C₃₈H₆₉N₅O₃·1/2H₂O: C, 77.99; H, 7.90; N, 7.84. Found: C, 77.85; H, 8.01; N, 7.76.

EXAMPLE 113

- 30 5-Carboxamido-2-ethyl-1,4-dihydro-4-(3-methoxyphenyl)-6-methyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)-pyridine (113). A mixture of 2-cyanoethyl propionylacetate (1.00 g, 5.91 mmol), m-anisaldehyde (1.0 ml, d 1.119, 8.22 mmol) and 3-
- 35 aminocrotonamide (0.89 g, 8.89 mmol) in EtOH (9 ml) was heated at reflux overnight. Then the solvent was evaporated to give an oily residue which was suspended in

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chloroform and flash chromatographed over silica gel (100 g). Elution with EtOAc/Hexane (1:2, 1:1 and 3:1) and EtOAc/MeOH (10:1) afforded an orange foam (0.782 g, 36% yield).

5

This foam (0.782 g, 2.12 mmol) was dissolved in EtOH (3 ml) and stirred with NaOH (0.121 g 3.03 mmol) in water (2 ml) for 3 h. The solution was acidified with 5% HCl and extracted with EtOAc (2 x 5 ml). The extract was washed
10 with saturated NaCl solution, dried (MgSO₄), filtered and concentrated to give a red gum (255 mg). It was dissolved in MeOH and flash chromatographed over silica gel (17 g) eluting with EtOAc/Hexane/MeOH (5:5:1) to give a yellow oil (88 mg, 13% yield).

15

This oil (85 mg, 0.27 mmol) was suspended in dry CH₂Cl₂ (5 ml) and treated with 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (52 mg, 0.27 mmol), 3-(4,4-diphenyl-piperidin-1-yl)propylamine (79 mg, 0.27 mmol)
20 and 4-dimethylamino-pyridine (2 mg). The mixture was stirred at room temperature overnight and then the solvent was evaporated. The residue was dissolved in chloroform and flash chromatographed over silica gel (17 g) eluting with EtOAc/MeOH/Et₃N (10:1:1) to give a pale
25 yellow foam (55 mg, 35% yield). Recrystallization from EtOAc/Hexane afforded a white solid (21 mg): mp 120-123°C. Anal. Calcd. for C₃₇H₄₄N₄O₃: C, 74.97; H, 7.48; N, 9.45. Found: C, 74.89; H, 7.61; N, 9.40.

30

EXAMPLE 114

4-(4-Aminophenyl)-2-ethyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)-pyridine (114). A solution of 2-Ethyl-
35 1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)pyridine (135 mg, 0.22 mmol) in dry MeOH (4 ml) was

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treated with 10% Pd/C (20 mg) and hydrogenated at 1 atm overnight. Then more catalyst (20 mg) was added and hydrogenation was continued overnight. Filtration of the reaction mixture through Celite afforded a yellow oil.

- 5 It was dissolved in chloroform and flash chromatographed over silica gel (16 g) eluting with EtOAc/Hexane/MeOH/Et₃N (40:20:3:3) to give a white foam (60 mg, 47% yield). The foam was dissolved in EtOAc/Hexane and treated with 1N HCl in ether (0.3 ml). The solvent was then evaporated
- 10 to afford a yellow solid: mp 169-172°C (dec). Anal. Calcd. for C₃₇H₄₄N₄O₃·2HCl·1/2H₂O: C, 65.87; H, 7.02; N, 8.30. Found: C, 65.80; H, 7.17; N, 8.31.

EXAMPLE 115

15

- 5-Carboxamide-1,4-dihydro-4-(4-methanesulfonylphenyl)-2,6-dimethyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamide)-pyridine (115). p-Methanesulfonyl-benzaldehyde (1.00 g, 5.43 mmol) was mixed with
- 20 cyanoethyl acetoacetate (0.84 g, 5.41 mmol), acetic acid (16 ul, d 1.049, 0.28 mmol) and piperidine (27 ul, d 0.861, 0.27 mmol) in 2-propanol (10 mL). The mixture was stirred at room temperature overnight. The solvent was replaced by EtOH (10 mL) which was then stirred at room
- 25 temperature for 2 h and then heated at reflux for 4 h. 3-Aminocrotonamide (0.543 g, 5.42 mmol) was added and the mixture heated at reflux overnight. The solvent was evaporated and the residue dissolved in EtOAc/MeOH/Et₃N (20:1:1) and flash chromatographed over silica gel (105
- 30 g) eluting with the same solvent to give a yellow foam (369 mg, 17% yield).

- The above foam (369 mg 0.91 mmol) was partially dissolved in EtOH (4 mL) and, with ice water bath cooling, treated
- 35 with NaOH (56 mg, 1.4 mmol) in water (1 mL). The mixture was stirred at room temperature for 3 h and the EtOH was evaporated. The aqueous layer was washed with CH₂Cl₂.

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twice and then acidified with 2N HCl to afford a precipitate which was filtered off as a yellow solid (235 mg, 73% yield).

- 5 The above yellow solid (233 mg, 0.66 mmol) was mixed with 3-(4,4-diphenylpiperidin-1-yl)-propylamine (197 mg, 0.67 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (129 mg, 0.67 mmol), and 4-dimethylamino-pyridine (82 mg, 0.67 mmol) in dry CH_2Cl_2 (8 mL) which was
10 then heated at reflux for 7 h. More carbodiimide (63 mg, 0.33 mmol) was added and the mixture was heated at reflux overnight. It was then diluted with CHCl_3 , washed with water twice and saturated NH_4Cl thrice, dried (MgSO_4) filtered and concentrated to give a yellow oil (385 mg).
15 This was dissolved in CHCl_3 and flash chromatographed over silica gel (20 g) eluting with $\text{EtOAc/MeOH/Et}_3\text{N}$ (20:1:1 then 20:2:1) to afford a yellow foam (209 mg). Trituration with hot EtOAc gave a pale yellow solid (140 mg, 34% yield): mp 206-209°C. Anal. Calcd. for
20 $\text{C}_{36}\text{H}_{42}\text{N}_4\text{O}_4\text{S} \cdot 3/4\text{H}_2\text{O}$: C, 67.53; H, 6.85; N, 8.75. Found: C, 67.51; H, 6.90; N, 8.51.

EXAMPLE 116

- 25 5-Carboxamido-2,6-diethyl-1,4-dihydro-4-(4-methanesulfonylphenyl)-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)-pyridine (116). p-Methanesulfonylbenzaldehyde (0.54 g, 2.93 mmol) was mixed with 2-cyanoethyl propionylacetate (0.50 g, 2.96 mmol), acetic
30 acid (9 μl , d 1.049, 0.16 mmol) and piperidine (14 μl , d 0.861, 0.14 mmol) in EtOH (6 mL). The suspension was stirred at room temperature overnight. A solution of 3-amino-2-propenamide (313 mg, 2.74 mmol) in EtOH (3 mL) was added and the mixture was heated at reflux overnight.
35 The solvent was evaporated to give a yellow oil which was dissolved in CHCl_3 and flash chromatographed over silica gel (70 g) eluting with $\text{EtOAc/Hexane/Et}_3\text{N}$ (15:5:1 then

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18:2:1) to afford a yellow foam (493 mg, 39% yield).

The above yellow foam (493 mg, 1.14 mmol) was dissolved in EtOH (5 mL), cooled by an ice water bath, and treated
5 with NaOH (74 mg, 1.85 mmol) in water (2 mL). The solution was stirred at room temperature for 2 h and then the EtOH was evaporated. The aqueous layer was diluted with water, washed twice with CH_2Cl_2 , cooled by an ice water bath and acidified with 2N HCl. Filtration gave a
10 pale yellow solid (329 mg, 76% yield): mp 137-140°C (dec).

The above yellow solid (326 mg, 0.86 mmol) was mixed with 3-(4,4-diphenyl-piperidin-1-yl)-propylamine (254 mg, 0.86 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide
15 hydrochloride (254 mg, 1.32 mmol), and 4-dimethylaminopyridine (105 mg, 0.86 mmol) in dry CH_2Cl_2 (12 mL) which was then heated at reflux overnight. CHCl_3 (6 mL) was added and the mixture was washed with water (2 x 5 mL) and saturated NH_4Cl solution (3 x 5 mL), dried
20 (MgSO_4), filtered and concentrated to give a pale brown foam (605 mg). It was dissolved in CHCl_3 and flash chromatographed over silica gel (37 g) eluting with EtOAc/MeOH/ Et_3N (20:1:1) to afford an off-white solid (338 mg, 60% yield). A portion (308 mg) was dissolved in EtOH
25 and treated with fumaric acid (55 mg) in EtOH. The solvent was evaporated and the residue recrystallized from 2-propanol to give a hygroscopic pale yellow solid (217 mg). Anal. Calcd. for $\text{C}_{38}\text{H}_{46}\text{N}_4\text{O}_4\text{S}\cdot\text{C}_4\text{H}_4\text{O}_4\cdot\text{C}_3\text{H}_8\text{O}\cdot\text{H}_2\text{O}$: C, 63.66; H, 7.12; N, 6.60. Found: C, 63.78; H, 7.01; N,
30 6.45.

EXAMPLE 117

5-Carboxamido-1,4-dihydro-4-(3-methoxyphenyl)-2,6-
35 dimethyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxamido)-pyridine (117). A mixture of benzyl acetoacetate (0.9 mL, 5.20 mmol), m-anisaldehyde

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(0.63 mL, 5.20 mmol), 3-aminocrotoamide (521 mg, 5.20 mmol) in 2-propanol (10 mL) was refluxed for 4 days. The solvent was removed and the solid residue was chromatographed (Flash silica; EtOAc : MeOH : 2M NH₃ in MeOH = 10 : 1 : 0.5) to give a solid which was chromatographed again (Flash silica, EtOAc) to give a yellow solid (643 mg, 32%).

At room temperature a suspension of Pd/C (81 mg, 10%, 0.076 mmol) in MeOH (5 mL) was flushed with argon, then treated with a solution of the above yellow solid (287 mg, 0.731 mmol) in MeOH (5 mL). The resulting mixture was flushed with H₂ then stirred under H₂ (balloon) for 3.5 hrs. The reaction mixture was filtered through celite and concentrated to afford a white solid (120 mg, 54%).

A mixture of the above white solid (120.0 mg, 0.3969 mmol), 3-(4,4-diphenylpiperidin-1-yl)propylamine (116.9 mg, 0.3969 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (85.4 mg, 0.446 mmol), and 4-dimethylaminopyridine (cat) in dry CH₂Cl₂ (10 mL) was stirred at room temperature for 14 hrs. The reaction mixture was then washed with saturated aqueous NaHCO₃ solution, dried, and concentrated. The resulting material was chromatographed (Flash silica, EtOAc : MeOH : 2M NH₃ in MeOH = 10 : 1 : 0.5) to give a solid, which was recrystallized from CH₂Cl₂ and EtOAc to afford white crystals (40 mg, 17%) 157-3: m. p. 212.0-213.0 °C. Anal. Calcd. for C₃₈H₄₂N₄O₃: C, 74.71, H, 7.31, N, 9.68. Found: C, 74.49, H, 7.09, N, 9.45.

EXAMPLE 118

35 3-Carboxamido-2-ethyl-1,4-dihydro-4-(4-methanesulfonylphenyl)-6-methyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)carboxyamido)-pyridine (118). A mixture of

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benzyl acetoacetate (0.31 mL, 1.79 mmol), 4-methylsulfonylbenzaldehyde (330 mg, 1.79 mmol), trans-3-amino-2-pentenamide (204 mg, 1.79 mmol) in 2-propanol (10 mL) was refluxed for 3 days. The solvent was removed and
5 the liquid residue was chromatographed (Flash silica, EtOAc) to give a yellow solid (507 mg, 62%).

At R.T. a suspension of Pd/C (1.117 g, 10%, 1.07 mmol) in MeOH (5 mL) was flushed with argon, then treated with a
10 solution of the above yellow solid (500 mg, 1.10 mmol) in MeOH (10 mL). The resulting mixture was flushed with H₂ then stirred under H₂ (balloon) for 3 hrs. The reaction mixture was filtered through celite and concentrated to afford a yellow solid (220 mg, 69%).

15 A mixture of this yellow solid (220 mg, 0.604 mmol), 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (115 mg, 0.658 mmol), and 4-dimethylaminopyridine (80.4 mg, 0.658 mmol) in dry CH₂Cl₂ (10 mL)
20 was stirred at R.T. for 1 hr and then treated with 3-(4,4-diphenylpiperidin-1-yl)propylamine (176 mg, 0.598 mmol). The reaction mixture was stirred for 14 hrs and then washed with saturated aqueous NaHCO₃ solution, dried, and concentrated. The resulting material was
25 chromatographed (Flash silica, EtOAc : MeOH : 2M NH₃ in MeOH = 10 : 1 : 0.5) to give a solid, which was chromatographed again (Flash silica, EtOAc : MeOH = 12 : 1) to give a solid. The solid was recrystallized from EtOAc and Hex to afford white crystals (81 mg, 21%)
30 5: m. p. 182.0-183.0 °C. Anal. Calcd. for C₃₇H₄₄N₄O₄S.1/3H₂O: C, 68.70, H, 6.95, N, 8.66, S, 4.95. Found: C, 68.71, H, 6.97, N, 8.47, S, 5.19.

EXAMPLE 119

35

1,4-Dihydro-2,6-dimethyl-5-(N-methyl)carboxamido-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)prop-

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- yl))carboxamidopyridino (119). A suspension of 4-nitrobenzaldehyde (5.00 g, 33.0 mmol), 2-cyanoethyl acetoacetate (5.13 g, 33.0 mmol), piperidine (140 mg, 1.65 mmol) and acetic acid (99 mg, 1.7 mmol) in 150 ml of
- 5 2-propanol was stirred at r.t. for 48 hrs. Reaction mixture was filtered, the solid collected was dried in air to give 2-[(4-nitrophenyl)methylene]-3-oxobutanoic acid 2-cyanoethyl ester as a white powder (6.08 g, 64%). A solution of 2-[(4-nitrophenyl)methylene]-3-oxobutanoic
- 10 acid 2-cyanoethyl ester (4.29 g, 14.9 mmol) and 3-amino-N-methylcrotonamide (2.55 g, 22.3 mmol) in 50 ml of EtOH was refluxed for 36 hrs. After solvent was removed, the residue was dissolved in 250 ml of CHCl₃, washed with water (2x100 ml) and dried over Na₂SO₄. After filtration and
- 15 removal of solvent, 3-(2-cyanoethoxy) carbonyl-1,4-dihydro-2,6-dimethyl-5-(N-methyl) carboxamido-4-(4-nitrophenyl) pyridine was obtained as a yellow powder (7.96 g, 63%). The solution of 3-(2-cyanoethoxy) carbonyl-1,4-dihydro-2,6-dimethyl-5-(N-methyl) carboxamido-4-(4-
- 20 nitrophenyl) pyridine (2.00 g, 5.20 mmol) in 40 ml acetone was treated with 40 ml 1N KOH solution at 0°C for 45 min. The acetone was removed in vacuo and aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the yellow precipitation was collected by filtration, washed
- 25 with 10 ml of cold water and dried in vacuo. 1.53 g (89% yield) of 1,4-dihydro-2,6-dimethyl-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid was obtained as a yellow powder.
- 30 The solution of 1,4-dihydro-2,6-dimethyl-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (745 mg, 2.25 mmol), 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (690 mg, 3.60 mmol) and 4-dimethylaminopyridine (275 mg, 2.25 mmol) in 200 ml of
- 35 CH₂Cl₂ was stirred at r.t. for 1 hr, to the solution was added the solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (662 mg, 2.25 mmol) in 2 ml of CH₂Cl₂, the mixture

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was stirred at refluxing conditions overnight. The mixture was washed with water (50 ml), sat'd NH_4Cl (3x50 ml), 50 ml 10% K_2CO_3 and 100 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil
 5 was obtained, which was purified by chromatography (SiO_2 , MeOH: CHCl_3 :1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. A yellowish powder (1.06 g, 77.5 %) was obtained. M.p. 124 °C; Calcd. for $\text{C}_{36}\text{H}_{41}\text{N}_5\text{O}_4$: C 71.14, H 6.80, N 11.52; Found: C 70.88, H 6.55, N 11.34.

10

Part of 3-(2-cyanoethoxy) carbonyl-1,4-dihydro-2,6-dimethyl-5-(N-methyl) carboxamido-4-(4-nitrophenyl) pyridine was subjected to chiral chromatography and two enantiomers were separated, which were subsequently
 15 hydrolysed and coupled with 3-(4,4-diphenylpiperidin-1-yl)propylamine to give enantiomers of 1,4-dihydro-2,6-dimethyl-5-(N-methyl) carboxamido-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]} carboxamidopyridine:

20 (+)-isomer: $[\alpha]_D^{20} = +880$ (c 0.35, CHCl_3)
 (-)-isomer: $[\alpha]_D^{20} = -840$ (c 0.33, CHCl_3)

EXAMPLE 120

25 5-Carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]} carboxamidopyridine (120). 5-Carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid was prepared in the same method illustrated in Example
 30 119. It was obtained as a yellow powder.

The suspension of 5-carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (400 mg, 1.16 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide
 35 hydrochloride (225 mg, 1.16 mmol) in 50 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the suspension thus formed was added the solution of 3-(4,4-diphenylpiperidin-1-

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yl)propylamine (310 mg, 1.05 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (2x10 ml), 10 ml 10% K_2CO_3 and 10 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ mixture. A yellowish powder (340 mg, 47.5 %) was obtained. M.p. 121-123 °C; Calcd. for $\text{C}_{37}\text{H}_{43}\text{N}_5\text{O}_4$: C 71.47, H 6.97, N 11.26; Found: C 71.24, H 6.69, N 10.97.

EXAMPLE 121

5-Carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4-phenylpiperidin-1-yl)propyl]}carboxamido-pyridine (121). The suspension of 5-carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (90 mg, 0.26 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (50 mg, 0.26 mmol) in 15 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the suspension was added the solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (57 mg, 0.26 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (2x10 ml), 10 ml 10% K_2CO_3 and 10 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ mixture. A yellowish powder (86 mg, 61%) was obtained. M.p. 90-101 °C; Calcd. for $\text{C}_{31}\text{H}_{39}\text{N}_5\text{O}_4 \cdot 3/4\text{H}_2\text{O}$: C 66.59, H 7.30, N 12.52; Found: C 66.89, H 6.92, N 12.30.

EXAMPLE 122

35

5-Carboxamido-1,4-dihydro-3-(N-{1-[2-(3-indolyl)ethyl]piperidin-4-yl})carboxamido-2,6-dimethyl-4-(4-

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nitrophenyl)pyridino (122). The suspension of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (326 mg, 1.03 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (219 mg, 1.13 mmol) in 25 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the suspension was added the solution of 1-[2-(3-indolyl)ethyl]-4-aminopiperidine (250 mg, 1.03 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (2x20 ml), 20 ml 10% K_2CO_3 and 20 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , MeOH: CHCl_3 :1N NH_3 in MeOH, 6:90:3) and precipitated by $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ mixture. A yellowish powder (134 mg, 23.8%) was obtained. M.p. 135-138 °C; Calcd. for $\text{C}_{29}\text{H}_{34}\text{N}_6\text{O}_6 \cdot 1/2\text{H}_2\text{O}$: C 65.32, H 6.39, N 15.23; Found: C 65.41, H 5.96, N 15.21.

EXAMPLE 123

5-Carboxamido-2,6-diethyl-1,4-dihydro-3-(N-{1-[2-(3-indolyl)ethyl]piperidin-4-yl})carboxamide-4-(4-nitrophenyl)pyridino (123). The suspension of 5-carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (486 mg, 1.53 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (323 mg, 1.69 mmol) in 30 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the suspension was added the solution of 1-[2-(3-indolyl)ethyl]-4-aminopiperidine (373 mg, 1.53 mmol) in 3 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (2x20 ml), 20 ml 10% K_2CO_3 and 20 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , MeOH: CHCl_3 :1N NH_3 in MeOH, 6:90:3) and precipitated by $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ mixture. A yellowish powder (273 mg, 31.3%) was obtained. M.p. 130-

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135 °C; Calcd. for $C_{32}H_{36}N_6O_4 \cdot 1/2H_2O$: C 66.30, H 6.78, N 14.50; Found: C 66.49, H 6.75, N 14.26.

EXAMPLE 124

5 **5-Carboxamido-1,4-dihydro-3-(N-{3-[4-2-methoxy-phenyl]piperazin-1-yl}propyl})carboxamido-2,6-dimethyl-4-(4-nitrophenyl)pyridine (124).** The suspension of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)
10 pyridine-3-carboxylic acid (150 mg, 0.47 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (91 mg, 0.47 mmol) in 20 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the suspension was added the solution of 1-(2-methoxyphenyl)-4-(3-aminopropyl)piperazine (118 mg, 0.47
15 mmol) in 3 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (2x10 ml), 10 ml 10% K_2CO_3 and 10 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by
20 chromatography (SiO_2 , MeOH: $CHCl_3$:1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /Et₂O mixture. A yellow-green powder (80 mg, 31%) was obtained. M.p. 95-100 °C; Calcd. for $C_{29}H_{36}N_6O_5$: C 63.48, H 6.61, N 15.32; Found: C 63.20, H 6.64, N 15.03.

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EXAMPLE 125

5-Carboxamido-2,6-diethyl-1,4-dihydro-3-(N-{3-[4-(2-methoxyphenyl)piperazin-1-yl]propyl})carboxamido-4-(4-nitrophenyl)pyridine (125). The suspension of 5-carboxamido-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)
30 pyridine-3-carboxylic acid (150 mg, 0.43 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (83 mg, 0.43 mmol) in 20 ml of CH_2Cl_2 was stirred at r.t.
35 for 1 hr, to the suspension was added the solution of 1-(2-methoxyphenyl)-4-(3-aminopropyl)piperazine (108 mg, 0.43 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at

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refluxing conditions overnight. The mixture was washed with water (2x10 ml), 10 ml 10% K_2CO_3 and 10 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , MeOH: $CHCl_3$:1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /Et₂O mixture. A yellow-green powder (160 mg, 64.5%) was obtained. M.p. 90-95 °C; Calcd. for $C_{31}H_{40}N_6O_5 \cdot 1/2H_2O$: C 63.57, H 7.06, N 14.35; Found: C 64.00, H 7.02, N 13.99.

10

EXAMPLE 126

3-{N-[3-(4-Cyano-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-2,6-dimethyl-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (126). The suspension of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (100 mg, 0.30 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (58 mg, 0.30 mmol) in 20 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the suspension was added the solution of 3-(4-cyano-4-phenylpiperidin-1-yl)propylamine (69 mg, 0.30 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (2x10 ml), 10 ml 10% K_2CO_3 and 10 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , MeOH: $CHCl_3$:1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /Et₂O mixture. A yellowish powder (90 mg, 54%) was obtained. M.p. 110-115 °C; Calcd. for $C_{31}H_{36}N_6O_4$: C 66.88, H 6.52, N 15.10; Found: C 66.69, H 6.41, N 15.12.

EXAMPLE 127

5-Carboxamido-1,4-dihydro-2,6-diisopropyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (127). To 15 ml of boiling p-

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xylene was added a solution of 6-(2-propyl)-2,2-dimethyl-
 2H,4H-1,3-dioxin-4-one (165 mg, 0.97 mmol) and 3-(4,4-
 diphenylpiperidin-1-yl)propylamine (285 mg, 0.97 mmol) in
 10 ml p-xylene dropwise in about 15 min., during which
 5 time, about 20 ml of xylene was distilled off through a
 condenser. Heating was continued for an additional 45
 min. to distill most xylene. The remaining xylene was
 further removed by evaporation in vacuo. The product,
 isobutanoylacetic acid N-[3-(4,4-diphenylpiperidin-1-
 10 yl)propyl]amide, was used for the next reaction without
 further purification.

The solution of 3-amino-4-methyl-2-pentenamide (135 mg,
 1.06 mmol), 4-nitrobenzaldehyde (146 mg, 0.97 mmol) and
 15 isobutanoylacetic acid N-[3-(4,4-diphenylpiperidin-1-
 yl)propyl]amide (394 mg, 0.96 mmol) in 20 ml of 2-
 propanol was refluxed for 72 hrs. After the solvent was
 removed, the residue was purified by chromatography (SiO₂,
 MeOH: CHCl₃:1N NH₃ in MeOH, 6:90:3) to give a yellowish
 20 oil, which was precipitated by CH₂Cl₂/Et₂O mixture. 45 mg
 (7.1% yield) of yellowish powder was obtained. M.p. 76-
 80 °C; Calcd for C₃₉H₄₇N₅O₆·1/2H₂O: C 69.21, H 7.45, N
 10.35; Found: C 68.98, H 7.18, N 10.54.

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EXAMPLE 128

2,6-Dioctyl-1,4-dihydro-5-(N-octyl)carboxamide-4-(4-
 nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}
 carboxamidopyridino (128). A suspension of 4-nitro-
 30 benzaldehyde (18.3 g, 0.118 mol), 2-cyanoethyl
 propionylacetate (20.0 g, 0.118 mol), piperidine (503 mg,
 5.91 mmol) and acetic acid (355 mg, 5.91 mmol) in 230 ml
 of 2-propanol was stirred at r.t. for 48 hrs. Reaction
 mixture was filtered, the solid collected was dried in
 35 air to give 2-[(4-nitrophenyl)methylene]-3-oxopentanoic
 acid 2-cyanoethyl ester as a white powder (31.7 g, 89%).
 A solution of 2-[(4-nitrophenyl)methylene]-3-oxopentanoic

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acid 2-cyanoethyl ester (14.72 g, 48.7 mmol) and benzyl 3-aminocrotonate (10.00 g, 48.7 mmol) in 150 ml of EtOH was refluxed for 36 hrs. After solvent was removed, the residue was dissolved in 250 ml of CHCl_3 , washed with water
5 (2x100 ml) and dried over Na_2SO_4 . After filtration and removal of solvent, 3-benzyloxycarbonyl-5-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine was obtained as a yellow oil (23.0 g, 96%).

10 The solution of 3-benzyloxycarbonyl-5-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine (6.30 g, 13.0 mmol) in 250 ml of 4.4% (w/w) formic acid/MeOH mixture was stirred with Pd/C (10%, 6.0 g) for 30 min., the reaction was quenched by addition of 100 ml
15 of CHCl_3 . The mixture was filtered and concentration of filtrate give a yellow powder, which was dissolved in CHCl_3 , washed with water and 1N HCl. After filtration and removal of solvent, 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-5-
20 carboxylic acid was obtained as a yellow powder (4.5 g, 87%).

3-(2-Cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-5-carboxylic acid (2.50 g, 6.25
25 mmol); 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.40 g, 12.5 mmol) and 4-dimethylaminopyridine (760 mg, 6.25 mmol) in 200 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was added the solution of methylamine (40% solution, 2.5 ml), the
30 mixture was stirred at r.t. overnight. The mixture was washed with water (100 ml), sat'd NH_4Cl (3x50 ml), 50 ml 10% K_2CO_3 and 100 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-
35 nitrophenyl)pyridine was obtained as a yellowish powder (2.30 g, 89%). The solution of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-5-(N-methyl)carboxamido-

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4-(4-nitrophenyl)pyridine (890 mg, 2.15 mmol) in 15 ml acetone was treated with 10 ml 1N KOH solution at 0°C for 45 min. The acetone was removed in vacuo and aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the
 5 yellow precipitation was collected by filtration, washed with 10 ml of cold water and dried in vacuo. 510 mg (66% yield) of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine was obtained as a yellow powder.

10

The solution of 2,6-diethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (494 mg, 1.38 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (476 mg, 2.50 mmol) and 4-
 15 dimethylaminopyridine (169 mg, 1.38 mmol) in 50 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was added the solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (405 mg, 1.38 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight.
 20 The mixture was washed with water (30 ml), sat'd NH_4Cl (3x20 ml), 20 ml 10% K_2CO_3 and 20 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by
 25 CH_2Cl_2 /hexane mixture. A yellowish powder (700 mg, 74%) was obtained. M.p. 123-126 °C; Calcd. for $\text{C}_{25}\text{H}_{33}\text{N}_5\text{O}_4 \cdot \text{H}_2\text{O}$: C 69.81, H 7.25, N 10.71; Found: C 69.79, H 7.05, N 10.74.

EXAMPLE 129

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2,6-Diethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (129). The solution of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-
 35 nitrophenyl)pyridine-5-carboxylic acid (350 mg, 0.90 mmol, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (260 mg, 13.5 mmol and 4-dimethyl-

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aminopyridine (110 mg, 0.90 mmol) in 20 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was added the solution of ethylamine (0.22 ml, 70% aqueous solution), the mixture was stirred at r.t. overnight. The mixture
5 was washed with water (10 ml), saturated aqueous NH_4Cl (3 x 10 ml), 20 ml 10% K_2CO_3 and 10 ml of brine. After drying with Na_2SO_4 and removal of solvent, 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)pyridine was obtained as a
10 yellowish powder (167 mg, 44%).

The solution of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)pyridine (167 mg, 0.39 mmol) in 10 ml acetone was treated
15 with 5 ml 1N KOH solution at 0° for 45 min. The acetone was removed in vacuo and aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the yellow precipitation was collected by filtration, washed with 10 ml of cold water and dried in vacuo. 118 mg (81% yield) of 2,6-
20 diethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid was obtained as a yellow powder.

The solution of 2,6-diethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (110 mg, 0.30 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (104 mg, 0.54 mmol) and 4-dimethylaminopyridine (40 mg, 0.30 mmol) in 20 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was
30 added the solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (88 mg, 0.30 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (10 ml), sat'd NH_4Cl (3x20 ml), 20 ml 10% K_2CO_3 and 20 ml of sat'd brine. After
35 drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , MeOH: CHCl_3 :1N NH_3 in MeOH, 6:90:3) and precipitated by

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CH_2Cl_2 /hexane mixture. A yellowish powder (115 mg, 49%) was obtained. M.p. 101-104 °C; Calcd. for $\text{C}_{39}\text{H}_{47}\text{N}_5\text{O}_4 \cdot 3/4\text{H}_2\text{O}$: C 70.62, H 7.37, N 10.56; Found: C 70.58, H 6.90, N 10.65.

5

EXAMPLE 130

2,6-Diethyl-1,4-dihydro-4-(4-nitrophenyl)-5-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine-3-carboxylic acid (130). The solution of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-5-carboxylic acid (395 mg, 1.00 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (345 mg, 1.80 mmol) and 4-dimethylaminopyridine (122 mg, 1.00 mmol) in 40 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was added the solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (294 mg, 1.00 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (20 ml), sat'd NH_4Cl (3x20 ml), 20 ml 10% K_2CO_3 and 20 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , MeOH: CHCl_3 :1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. 3-(2-Cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-5-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (552 mg, 82%).

The solution of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-5-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (500 mg, 0.82 mmol) in 15 ml acetone was treated with 8.0 ml 1N KOH solution at 0°C for 45 min. The acetone was removed in vacuo and aqueous layer was acidified to pH=4 by 2N hydrochloric acid, the yellow precipitation was collected by filtration and dried in vacuo. 340 mg (75% yield) of

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product was obtained as a yellowish powder. M.p. 154-158 (dec) °C; Calcd. for $C_{37}H_{42}N_6O_5 \cdot 3/4H_2O$: C 69.85, H 6.89, N 8.81; Found: C 69.82, H 6.70, N 8.88.

5

EXAMPLE 131

5-(N-Ethyl)carboxanido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (131). A suspension of
10 4-nitrobenzaldehyde (10.00 g, 66.2 mol), 2-cyanoethyl acetoacetate (10.27 g, 66.2 mol), piperidine (281 mg, 3.31 mmol) and acetic acid (198 mg, 3.31 mmol) in 250 ml of 2-propanol was stirred at r.t. for 48 hrs. Reaction mixture was filtered, the solid collected and dried in
15 air to give 2-cyanoethyl 2-[(4-nitrophenyl)methylene]-3-oxobutanate as a white powder (11.24 g, 59%).

A solution of 2-cyanoethyl 2-[(4-nitrophenyl)methylene]-3-oxobutanate (15.06 g, 52.3 mmol) and benzyl 3-amino-
20 crotonate (10.00g, 52.3 mmol) in 150 ml of EtOH was refluxed for 36 hrs. After solvent was removed, the residue was dissolved in 250 ml of $CHCl_3$, washed with water (2 x 100 ml) and dried over Na_2SO_4 . After filtration and removal of solvent, 3-benzylloxycarbonyl-5-(2-cyano-
25 ethoxy)carbonyl-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine was obtained as a yellow oil (23.4 g, 97%).

The solution of 3-benzylloxycarbonyl-5-(2-cyanoethoxy)carbonyl-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine (3.24 g, 7.02 mmol) in 160ml of 4.4%
30 (w/w) formic acid/MeOH mixture was stirred with Pd/C (10%, 3.24 g) for 30 min., the reaction was quenched by addition of 10 ml of $CHCl_3$. The mixture was filtered and concentration of filtrate, give a yellow powder, which was
35 dissolved in $CHCl_3$, washed with water and 1N HCL. After drying and removal of solvent, 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-5-

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carboxylic acid was obtained as a yellow powder (1.94 g, 75%).

5 The solution of 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-5-carboxylic acid (500 mg, 1.35 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (532 mg, 2.69 mmol) and 4-dimethylaminopyridine (164 mg, 1.35 mmol) in 50 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was
10 added the solution of ethylamine (434 mg, 70% aqueous solution), the mixture was stirred at r.t. overnight. The mixture was washed with water (30 ml), saturated aqueous NH_4Cl (3 x 25) ml, 25 ml of 10% aqueous K_2CO_3 and 30 ml of brine. After drying with Na_2SO_4 and removal of
15 solvent, 3-(2-cyanoethoxy)carbonyl-5-(N-ethyl)carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine was obtained as a yellowish powder (529 mg 98%).

The solution of 3-(2-cyanoethoxy)carbonyl-5-(N-ethyl)carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine (535 mg, 1.35 mmol) in 10 ml acetone
20 was treated with 10 ml 1N KOH solution at 0°C for 45 min. The acetone was removed in vacuo and aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the yellow precipitation was collected by filtration, washed with 5
25 ml of cold water and dried in vacuo. 5-(N-ethyl)carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid was obtained as a yellow powder (266 mg, 57%).

30

The suspension of 5-(N-ethyl)carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (285 mg, 0.825 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (315 mg, 1.65 mmol) and 4-
35 dimethylaminopyridine (101 mg, 0.825 mmol) in 20 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was added the solution of 3-(4,4-diphenylpiperidin-1-

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yl)propylamine (243 mg, 0.825 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (10 ml), sat'd NH_4Cl (3x20 ml), 20 ml 10% K_2CO_3 and 20 ml of sat'd brine. After
5 drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. A yellowish powder (190 mg, 37%) was obtained. M.p. 104-108 °C; Calcd. for $\text{C}_{37}\text{H}_{43}\text{N}_5\text{O}_4$: C
10 71.47, H 6.97, N 11.26; Found: C 71.21, H 6.88, N 11.27.

EXAMPLE 132

2,6-Diethyl-1,4-dihydro-3-(N-isopropyl)carboxamido-4-(4-nitrophenyl)-5-(N-[3-(4,4-diphenylpiperidin-1-yl)propyl])carboxamidopyridine (132). The solution of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-5-carboxylic acid (395 mg, 1.00 mmol),
15 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (345 mg, 1.80 mmol) and 4-dimethylaminopyridine (122 mg, 1.00 mmol) in 20 ml of CH_2Cl_2 stirred at r.t. for 1 hr, to the solution was added the solution of isopropylamine (300 mg, 5.00 mmol), the mixture was stirred at r.t. overnight. The mixture was
20 washed with water (10 ml), saturated aqueous NH_4Cl (3 x 10 ml), 20 ml 10% K_2CO_3 and 10 ml of brine. After drying with Na_2SO_4 and removal of solvent, 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-5-(N-isopropyl)carboxamido-4-(4-nitrophenyl)pyridine was obtained as a yellowish
25 powder (345 mg, 80%).

The solution of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-5-(N-isopropyl)carboxamido-4-(4-nitrophenyl)pyridine (300 mg, 0.69 mmol) in 15 ml acetone was
35 treated with 5 ml 1N KOH solution at 0° for 45 min. The acetone was removed in vacuo and aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the yellow

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precipitation was collected by filtration, washed with 10 ml of cold water and dried in vacuo. 220 mg (83% yield) of 2,6-diethyl-1,4-dihydro-5-(N-isopropyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid was obtained as
5 a yellow powder.

The suspension of 2,6-diethyl-1,4-dihydro-5-(N-isopropyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (210 mg, 0.55 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (210 mg, 1.00 mmol) and
10 4-dimethylaminopyridine (70 mg, 0.60 mmol) in 20 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was added the solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (161 mg, 0.55 mmol) in 2 ml of CH_2Cl_2 , the
15 mixture was stirred at refluxing conditions overnight. The mixture was washed with water (10 ml), sat'd NH_4Cl (3x20 ml), 20 ml 10% K_2CO_3 and 20 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 ,
20 MeOH: CHCl_3 :1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. A yellowish powder (212 mg, 58%) was obtained. M.p. 201 °C (dec.); Calcd. for $\text{C}_{40}\text{H}_{49}\text{N}_5\text{O}_4 \cdot 1/2\text{H}_2\text{O}$: C 71.40, H 7.49, N 10.41; Found: C 71.39, H 7.32, N 10.63.

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EXAMPLE 133

2,6-Diethyl-1,4-dihydro-4-(4-nitrophenyl)-5-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamido-3-(N-propyl)carboxamidopyridine (133). The solution of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-5-carboxylic acid (395 mg, 1.00 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (345 mg, 1.80 mmol) and 4-dimethylaminopyridine (122 mg, 1.00 mmol) in 20 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was added the solution of propylamine (300 mg, 5.00 mmol), the mixture
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was stirred at r.t. overnight. The mixture was washed with water (10 ml), saturated aqueous NH_4Cl (3 x 10 ml), 20 ml 10% K_2CO_3 and 10 ml of brine. After drying with diethyl-1,4-dihydro-4-(4-nitrophenyl)-5-(N-propyl)carboxamidopyridine was obtained as a yellowish powder (420 mg, 95%).

The solution of 3-(2-cyanoethoxy)carbonyl-2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)-5-(N-propyl)carboxamidopyridine (420 mg, 0.95 mmol) in 10 ml acetone was treated with 5 ml 1N KOH solution at 0° for 45 min. The acetone was removed in vacuo and aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the yellow precipitation was collected by filtration, washed with 10 ml of cold water and dried in vacuo. 276 mg (75% yield) of 2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)-5-(N-propyl)carboxamidopyridine-3-carboxylic acid was obtained as a yellow powder.

The suspension of 2,6-diethyl-1,4-dihydro-4-(4-nitrophenyl)-5-(N-propyl)carboxamidopyridine-3-carboxylic acid (250 mg, 0.645 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (247 mg, 1.29 mmol) and 4-dimethylaminopyridine (80 mg, 0.65 mmol) in 20 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was added the solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (190 mg, 0.645 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (10 ml), sat'd NH_4Cl (3x20 ml), 20 ml 10% K_2CO_3 and 20 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , MeOH: CHCl_3 :1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. A yellowish powder (180 mg, 42%) was obtained. M.p. 120-123 °C; Calcd. for $\text{C}_{40}\text{H}_{49}\text{N}_5\text{O}_4 \cdot \text{H}_2\text{O}$: C 71.40, H 7.49, N 10.41; Found: C 71.14, H 7.21, N 10.51.

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EXAMPLE 134

1,4-Dihydro-2,6-dimethyl-4-(4-nitrophenyl)-5-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamido-3-(N-propyl)carboxamidopyridine (134). The solution of 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-5-carboxylic acid (500 mg, 1.35 mmol), 1-(3-dimethylaminopropyl)-3-ethylaminopyridine (164 mg, 1.35 mmol) in 50 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was added the solution of propylamine (164 mg, 1.35 mmol), the mixture was stirred at r.t overnight. The mixture was washed with water (30 ml), saturated aqueous NH_4Cl (3 x 25 ml), 25 ml of 10% aqueous K_2CO_3 and 30 ml of brine. After drying with Na_2SO_4 and removal of solvent, 3-(2-cyanoethoxy) carbonyl-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-5-(N-propyl)carboxamidopyridine was obtained as a yellowish powder (555 mg 100%).

The solution of 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-5-(N-propyl)carboxamidopyridine (500 mg, 1.20 mmol) in 10 ml acetone was treated with 5 ml 1N KOH solution at 0°C for 45 min. The acetone was removed in vacuo and aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the yellow precipitation was collected by filtration, washed with 5 ml of cold water and dried in vacuo. 1,4-Dihydro-2,6-dimethyl-4-(4-nitrophenyl)-5-(N-propyl)carboxamidopyridine-3-carboxylic acid was obtained as a yellow powder (275 mg, 64%).

The suspension of 1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-5-(N-propyl)carboxamidopyridine-3-carboxylic acid (240 mg, 0.582 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (223 mg, 1.16 mmol) and 4-dimethylaminopyridine (71 mg, 0.58 mmol) in 20 ml of CH_2Cl_2 was stirred at r.t. for 1 hr, to the solution was added the solution of 3-(4,4-diphenylpiperidin-1-

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yl)propylamine (171 mg, 0.58 mmol) in 2 ml of CH_2Cl_2 , the mixture was stirred at refluxing conditions overnight. The mixture was washed with water (10 ml), sat'd NH_4Cl (3x20 ml), 20 ml 10% K_2CO_3 and 20 ml of sat'd brine. After drying with Na_2SO_4 and removal of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. A yellowish powder (190 mg, 51%) was obtained. M.p. 142-145 °C; Calcd. for $\text{C}_{25}\text{H}_{25}\text{N}_3\text{O}_8\cdot\text{H}_2\text{O}$: C 69.81, H 7.25, N 10.71; Found: C 70.12, H 6.85, N 11.01.

EXAMPLE 135

Ethyl 4-Methoxy-3-oxo-butanate. A mixture of 15.8 g of ethyl 4-chloroacetate (96.2 mmol) and 3.39 g of methanol (106 mmol) in 10 mL of THF were added dropwise to a stirred suspension of 4.62 g of 60% NaH (in mineral oil), 1.60 g of NaI (9.62 mmol), and 3.10 g of tetrabutylammonium bromide (9.62 mmol) in 40 mL of THF at -30 °C over a period of 1.5 hrs. The reaction mixture was then warmed to room temperature and stirred for 4 days. The reaction mixture was cooled to -30 °C, quenched with 5 mL of methanol, and warmed to room temperature. The reaction mixture was poured into 0.5 L of 10% HCl solution, extracted with 2 x 100 mL of EtOAc, dried (Na_2SO_4), and the solvent was removed in vacuo. The crude product was distilled. The fraction boiling at 65-70 °C (0.3 mm Hg) was collected and used in the next experiments after spectral characterization.

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3-(Benzyloxy)carbenyl-5-(2-cyanoethoxy)carbenyl-6-ethyl-1,4-dihydro-2-(methoxy)methyl-4-(4-nitro)phenylpyridine. A mixture of 3.28 g of ethyl 4-methoxy-3-oxo-butanate (20.5 mmol) and 4.43 g of benzyl alcohol (41.0 mmol) were heated at 140-150 °C (10-15 mm Hg) for 2 hrs. The reaction mixture was cooled, diluted with 20 mL of ethanol (denatured), 1.90 g of ammonium acetate (24.6

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mmol) was added, and the resulting mixture was heated at reflux temperature for 1.5 hrs. The reaction mixture was cooled and 5.27 g of 2-cyanoethyl 2-(4-nitro)phenylmethyleno-3-oxopentanoate was added to the
 5 reaction mixture. The resulting mixture was heated at reflux temperature for 2 hrs, cooled, and solvent was removed in vacuo. The crude product was chromatographed on 550 g of silica packed with 10% EtOAc-hexane. The column was eluted with 20% (2 L), and 30% EtOAc-hexane (4
 10 L) to give 3.08 g (30%) of the title compound as a yellow oil with solidified on standing. The product was used in the next step after spectral characterization.

5-(2-Cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-(methoxy)methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid. A suspension of 2.86 g of 3-(benzyloxy)carbonyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-(methoxy)methyl-4-(4-nitro)phenylpyridine (5.66 mmol), 572 mg of 10% Pd/C, 70 mL of methanol, and 2.09 mL of formic acid
 20 were stirred at room temperature for 0.5 h. The reaction mixture was diluted with 30 mL of chloroform, filtered through a pad of Celite 545. The filtrate was concentrated in vacuo, and the residue was chromatographed on 250 g of silica packed with 30% EtOAc-hexane. The column was eluted with 50% to 80% EtOAc-hexane (10% change/1 L) to give 1.33 g of the title compound (57%) as a yellow oily solid. Anal. Calc. for $C_{28}H_{27}N_3O_7$: C, 57.83; H, 5.10; N, 10.12. Found: C, 57.78; H, 5.08; N, 9.99.

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5-(2-Cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-(methoxy)methyl-4-(4-nitro)phenyl-3-(N-(3,4,4-diphenylpiperidin-1-yl)propyl)carboxamidopyridine, monohydrate. A solution of 433 mg of 5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-(methoxy)methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (1.04 mmol),
 35 401 mg of 1-(dimethylaminopropyl)-3-ethylcarbodiimide

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hydrochloride (DMAPECD) (2.09 mmol), and 153 mg of 4-dimethylaminopyridine (DMAP) (1.25 mmol) in 5 mL of dry dichloromethane were stirred at room temperature for 1 h. The reaction mixture was charged with 328 mg of N-(3-aminopropyl)-4,4-diphenylpiperidine (1.25 mmol), and the resulting solution was heated at reflux temperature for 2 hrs. The reaction mixture was cooled, and applied to 200 g of silica packed with 5% MeOH-EtOAc. The column was eluted with 10% to 20% MeOH-EtOAc (1 L/5% change) to afford 552 mg of the title compound (77%) as a yellow foamy solid: mp 120-125 °C; Anal. Calc. for $C_{40}H_{45}N_5O_6 \cdot 0.5H_2O$: C, 68.55; H, 6.62; N, 9.99. Found: C, 68.37; H, 6.26; N, 9.98.

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EXAMPLE 136

6-Ethyl-1,4-dihydro-2-(methyloxy)methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-carboxylic acid (136). A solution of 40 mg of NaOH in 2 mL of water was added to 530 mg of 5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-(methyloxy)methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (0.766 mmol) in 10 mL of dioxane. The resulting mixture was stirred at room temperature for 1 hour. The solvent was removed in vacuo, the residue was partitioned between 20 mL of water (containing 200 mg of NaOH) and EtOAc (10 mL), separated, and the organic layer was extracted with 2 X 5 mL of water. The combined aqueous extracts were acidified (concentrated HCl, pH = 3-4), and the precipitated oil was extracted with 3 X 10 mL of dichloromethane. The combined organic extracts were dried (Na_2SO_4), and the solvent was removed in vacuo to afford 472 mg (97%) of the title compound as a yellow solid: mp 120-125 °C (decomp.); Anal. Calcd for $C_{37}H_{42}N_6O_6 \cdot 2H_2O$: C, 65.86, H, 6.87; N, 8.30. Found: C, 65.52; H, 7.05; N, 7.89.

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EXAMPLE 137

5-Carboxamido-6-ethyl-1,4-dihydro-2-(methyloxy)methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine, Hemihydrate (137). A mixture of 70.0 mg of 6-ethyl-1,4-dihydro-2-(methyloxy)methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-carboxylic acid (0.110 mmol), 90.5 mg of dicyclohexylcarbodiimide (DCC) (0.435 mmol), and 16.0 mg of DMAP (0.132 mmol) in 5 mL of dry dichloromethane were stirred at room temperature for 1 hour followed by addition of 5 mL of concentrated ammonia. The resulting mixture was heated at reflux temperature for 16 hours, cooled, filtered, dichloromethane was removed in vacuo, and the residue was dissolved in 5 mL of ethyl acetate (a small amount of dichloromethane was added to make the mixture homogeneous). The ethyl acetate solution was sequentially washed with aqueous saturated ammonium chloride solution (3 X 2 mL), aqueous sodium carbonate solution (2 mL), dried (Na_2SO_4), and the solvent was removed in vacuo. The residue was chromatographed on 200 g of silica packed with NH_3 (2 M in MeOH)-MeOH- CHCl_3 (1:2:40). The column was eluted with the same solvent to give 21.0 mg of the title compound as a yellow solid: mp 89 °C (decomp.); Anal. Calc. for $\text{C}_{37}\text{H}_{43}\text{N}_5\text{O}_5 \cdot 0.5 \text{ H}_2\text{O}$: C, 68.72; H, 6.86; N, 10.85. Found: C, 68.40; H, 6.91; N, 10.41

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EXAMPLE 138

Ethyl 4-(2,2,2-trifluoroethyl)oxy-3-oxobutanoate. A solution of 5.00 g of trifluoroethanol (50.0 mmol) in 5 mL of dry THF was added dropwise, over a period of 0.5 hr, to a stirred mixture of 4.00 g of 60% dispersion of NaH (100 mmol), 1.61 g of tetrabutylammonium bromide (5.0 mmol), and 830 mg of NaI (5.0 mmol) in 20 mL of dry THF

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(water bath). The resulting mixture was stirred for 0.5 hrs, cooled to -30 °C, and a solution of 8.23 g of ethyl 4-chloro-3-oxobutanoate (50.0 mmol) in 10 mL of dry THF was added dropwise, over a period of 15 min, to the
5 reaction mixture. The reaction mixture was warmed to 0 °C over a period of 2 hrs, and stirred at room temperature for 36 hrs. The reaction mixture was quenched with 5 mL of ethanol, partitioned between 100 mL of EtOAc and 100 mL of 10% aqueous HCl solution, separated, extracted with 2
10 x 40 mL of EtOAc, the combined organic extracts were dried (Na₂SO₄), and the solvent was removed in vacuo. The crude product was chromatographed on 400 g of silica packed with 5% EtOAc-hexane. The column was eluted with 5 to 25% EtOAc-hexane (1 L/5% change) to afford 8.75 g
15 (77%) of ethyl 4-(2,2,2-trifluoroethyl)oxy-3-oxobutanoate as a slightly yellow oil. The product was used in the next step after spectral characterization.

2-Cyanoethyl 4-(2,2,2-trifluoroethyl)oxy-3-oxobutanoate.
20 A mixture of 4.04 g of ethyl 4-(2,2,2-trifluoroethyl)oxy-3-oxobutanoate (17.7 mmol) and 2.55 g of 3-hydroxypropionitrile (35.9 mmol) was heated at reflux temperature at a bath temperature of 135-150 °C at 10 torr for 6 hrs. The reflux condensor was replaced with a
25 distillation head and the product was distilled under reduced pressure to give 4.26 g (96%) of the desired product as a viscous oil: bp 155-158 °C (1.5). The product was used in the next step after spectral characterization.

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5-Carboxamide-2-((2,2,2-trifluoroethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridino-3-carboxylic acid. A mixture of 1.07 g of 2-cyanoethyl 4-(2,2,2-trifluoroethyl)oxy-3-oxobutanoate (4.23 mmol) and 391 mg
35 of ammonium acetate (5.08 mmol) in 5 mL of ethanol were heated at reflux temperature for 15 min, cooled, 2-(4-nitro)phenylmethylenoacetoacetamide (4.23 mmol) was added

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to the reaction mixture. The resulting mixture was heated at reflux temperature for 4.5 hours, cooled, and a solution of 406 mg of NaOH (10.2 mmol) in 5 mL of water was added to the reaction mixture. The resulting mixture was stirred at room temperature for 0.5 hour. The solvent was removed in vacuo, and the residue was partitioned between EtOAc (20 mL) and water (20 mL containing 300 mg of NaOH), separated, and the organic layer was extracted with 2 X 10 mL of water (each containing 150 mg of NaOH). The combined aqueous extracts were filtered, acidified to pH 2-3 with concentrated HCl, and the separated oil was extracted with 50 and then 2 X 20 mL of EtOAc. The combined EtOAc extracts were dried (MgSO₄), and the solvent was removed in vacuo. The crude product crystallized upon trituration with ethyl acetate to give 450 mg of the title compound (268) as a yellow crystalline solid: mp 184 °C (decomp.); Anal. Calc. for C₁₇H₁₆N₃F₃O₆: C, 49.16; H, 3.88; N, 10.12. Found: 48.81; H, 3.97; N, 9.80.

5-Carboxamide-2-(2,2,2-trifluoroethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carbamidopyridino (138). A mixture of 102 mg of 6-methyl-4-(4-nitrophenyl)-2-((2,2,2-trifluoroethyl)oxy)methyl-5-carboxamido-1,4-dihydropyridine-3-carboxylic acid (0.230 mmol), 72.0 mg of 1-(3-amino)propyl-4,4-diphenylpiperidine (0.276 mmol), 119 mg of DCC (0.575 mmol), and 31.0 mg of DMAP (0.253 mmol) in 5 mL of dry dichloromethane were heated at reflux temperature for 3 hours, cooled, filtered, and the solvent was removed in vacuo. The residue was dissolved in 5 mL of EtOAc, and sequentially washed with saturated aqueous ammonium chloride solution (2 X 2 mL), saturated aqueous sodium carbonate solution (2 mL), dried (Na₂SO₄), and directly applied to 200 g of silica packed with 2N NH₃ (in methanol)-MeOH-CHCl₃ (1:2:20). The column was eluted with the same solvent system to afford 140 mg of product

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as a yellow solid (87%): mp 89 °C (decomp.); Anal. Calc. for $C_{17}H_{20}N_5F_3O_5$: C, 64.24; H, 5.83; N, 10.12. Found: C, 63.90; H, 5.87; N, 9.66

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EXAMPLE 139

2-Azidoethanol (100% reagent grade; IX): A mixture of 55.6 g of sodium azide (0.855 mol), and 81.4 g of bromoethanol (1) (0.649 mol), and 394 mg of sodium hydroxide (9.85 mmol) in 250 mL of water as stirred in a 61-64 °C bath for 24 hours. The reaction mixture was saturated with solid sodium sulfate, extracted with 250 mL and then 10 X 100 mL of EtOAc. The combined EtOAc extracts were dried (Na_2SO_4), solvent removed in vacuo, redissolved in 250 mL of EtOAc, redried ($MgSO_4$), and the solvent removed in vacuo. The crude product was distilled under reduced pressure to give 45.1 g of 2-azidoethanol (80%) as a colorless oil. The product was used in the next step after spectral characterization: bp 40-45°C (0.5 mmHg).

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t-Butyl 4-(2-Azidoethyl)oxy-3-oxobutanoate (V):

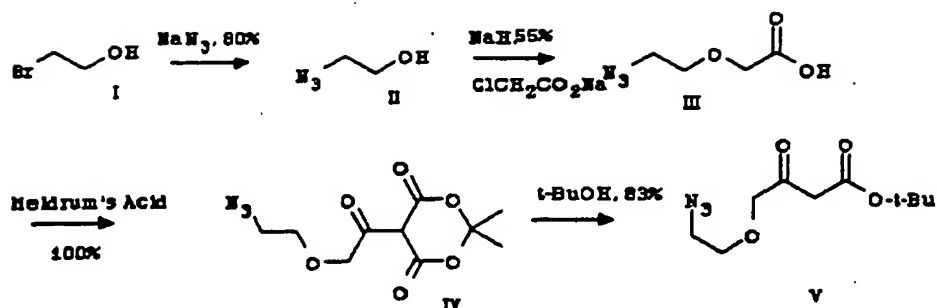
(2-Azidoethyl)oxynicotinic Acid (XII): A solution of 50.0 g of 2-azidoethanol (574 mmol) in 100 mL of dry THF was added dropwise to a stirred (mechanical stirrer) suspension of 25.3 g of NaH (632 mmol), in 250 mL of dry THF over a period of 1 hour. The reaction mixture was charged with 18.5 g of tetrabutylammonium bromide (57.4 mmol) and 9.52 g of potassium iodide (57.4 mmol) in one portion. Finally, a solid addition funnel was used to add 73.6 g of sodium chloroacetate (632 mmol) to the reaction mixture. The resulting suspension was heated at reflux temperature for 20 hrs. The reaction mixture was quenched with 200 mL of water (added dropwise with cooling), and the THF was removed in vacuo. The resulting basic solution was washed with dichloromethane (8 X 200 mL). The aqueous extract was acidified to pH = 1 (concentrated HCl), saturated with solid NaCl, and

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extracted with 6 X 350 mL of dichloromethane. The combined dichloromethane extracts were dried overnight over Na_2SO_4 , solvent removed in vacuo to give 45.6 g of III as a yellow oil (55%). The product was used in the next coupling experiment after spectral characterization. Carbonyldiimidazole (9.83 g, 60.6 mmol) and (2-azidoethoxy)acetic acid (II) (8.00 g, 55.1 mmol) in 100 mL of dry dichloromethane were stirred at room temperature for 1 hour. A solution of 8.7 g of 2,2-dimethyl-1,3-dioxane-4,6-dione (60.6 mmol, Meldrum's acid) and 4.4 g of dry pyridine (55.1 mmol) in 30 mL of dry dichloromethane were added to the reaction mixture, and stirred for 16 hrs at room temperature. The reaction mixture was washed with aqueous 2 N HCl solution (2 X 60 mL), water (2 X 40 mL), and brine (40 mL), dried (MgSO_4), and the solvent removed under reduced pressure to give 15 g of the desired product (IV) (100%). TLC showed small amounts of Meldrum's acid in the crude product. The crude product was used in the next experiment without any further purification.

A solution of 8.25 g of IV (30.4 mmol) in 20 mL of t-BuOH was heated at reflux temperature for 2.5 hrs. The reaction mixture was cooled, concentrated in vacuo (7.40 g), and the crude product was filtered through a pad of silica (eluted with EtOAc-hexane, 1:4) to give 6.11 g of t-butyl 4-(2-azidoethyl)oxy-3-oxobutanoate (V) (83%). This product was spectroscopically pure, and was used in the next experiment without any further purification or characterization.

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2-((2-Azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-3-(1,1-dimethylethoxy)carbonyl-4-(4-nitro)phenylpyridine. A mixture of 1.00 g of t-butyl 4-(2-azidoethoxy)-3-oxopentanoate (4.10 mmol) and concentrated ammonia (0.800 g, 24.6 mmol) in 1.5 mL of t-BuOH was stirred at room temperature 17 hours. The solvent was removed in vacuo to give a yellow viscous oil which was used in the next step after spectral characterization. A mixture of the resulting enamide, and 0.850 g of 2-cyanoethyl 2-(4-nitro)phenylmethyleno-3-oxopentanoate in 15 mL of t-BuOH was heated at reflux temperature for 5 hrs. The reaction mixture was concentrated in vacuo, and the crude product was chromatographed on silica (EtOAc-hexane, 1:3) to give 836 mg of the title compound (56%) as a yellow viscous oil: Anal. Calc. for $\text{C}_{25}\text{H}_{30}\text{N}_6\text{O}_7$: C, 57.02; H, 5.25; N, 15.95. Found: C, 56.77; H, 5.67; N, 15.69.

2-((2-Azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(1,1-dimethylethoxy)carbonyl-4-(4-nitro)phenylpyridine-5-carboxylic acid. A solution of 91 mg of sodium hydroxide (2.3 mmol) in 7.5 mL of water was added to a solution of

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800 mg of 2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-3-(1,1-dimethylethoxy)carbonyl-4-(4-nitro)phenylpyridine (1.52 mmol) in 7.5 mL of dioxane. The resulting mixture was stirred at room temperature for 3.5 hours. The reaction mixture was washed with ether (10 mL), and the ether extract was back-washed with water (basic at pH = 9-10). The combined aqueous extracts were acidified (pH = 4), and the precipitated solid was collected to give the desired acid as a yellow solid (600 mg, 83%): mp 170-173 °C; Anal. Calc. for $C_{22}H_{27}N_5O_7$: C, 55.80; H, 5.76; N, 14.78. Found: C,

2-((2-Azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(1,1-dimethylethoxy)carbonyl-4-(4-nitro)phenyl-5-(N-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (139). A mixture of 300 mg of 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(1,1-dimethylethoxy)carbonyl-4-(4-nitro)phenylpyridine-5-carboxylic acid (0.634 mmol), 182 mg of DMAPECD, and 93 mg of DMAP in 8 mL of dry dichloromethane were stirred at room temperature for 3 hrs. The reaction mixture was charged with 216 mg of N-(3-aminopropyl)-4,4-diphenylpiperidine (0.824 mmol), and heated at reflux temperature for 19 hours. The reaction mixture was concentrated in vacuo and the crude product was chromatographed (5% MeOH-EtOAc) to give 400 mg of desired product (86%) as a yellow foamy solid: mp 62-67 °C; Anal. Calc. for $C_{42}H_{51}N_7O_6$: C, 67.26; H, 6.89; N, 13.07. Found: C, 66.96; H, 6.79; N, 12.87.

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EXAMPLE 140

2-((2-Aminoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(1,1-dimethylethoxy)carbonyl-4-(4-nitro)phenyl-5-(N-3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine, (140). A solution of 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(1,1-dimethylethoxy)carbonyl-4-(4-

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nitro)phenyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (0.180 mmol), 57 mg of triphenylphosphine (0.22 mmol), and 5 mL of water in 3.5 mL of ethyl acetate were stirred at room temperature for 13 hours. The reaction mixture was concentrated in vacuo and the crude product was chromatographed on silica (2N NH₃ (in methanol)-MeOH-CHCl₃, 1:1:9) to give 25 mg of the title compound as a light yellow foamy solid: mp 84-89 °C; Anal. Calcd for C₄₂H₃₃N₅O₆·0.7H₂O: C, 68.49; H, 7.44; N, 9.51. Found: C, 68.14; H, 7.00; N, 9.41.

EXAMPLE 141

2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-3-carboxylic acid. A mixture of 2.90 g of 2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-3-(1,1-dimethylethoxy)carbonyl-4-(4-nitro)phenylpyridine (5.51 mmol) in 10 mL of formic acid was stirred for 1.5 hours, solvent removed in vacuo. The crude product was triturated with EtOAc and a small amount of hexane and the resulting precipitated yellow product was collected (700 mg): mp 150 °C (decomp.). The product was used in the following steps after spectral characterization.

2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (141). A solution of 700 mg of 2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-3-carboxylic acid (1.49 mmol), 461 mg of DCC (2.23 mmol), and 145 mg of DMAP (1.19 mmol) in 10 mL of dry dichloromethane were stirred at room temperature for 1.5 hours. The reaction mixture was charged with 570 mg of N-(3-aminopropyl)-4,4-diphenylpiperidine (1.93 mmol), and the reaction mixture was stirred for 13 hours. The reaction mixture was

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filtered and applied to a flash chromatography column (silica, MeOH-EtOAc 5% to 10%) to give 815 mg of the desired product (73%) as a yellow foamy solid: mp 63-67 °C; Anal. Calcd for $C_{41}H_{46}N_8O_6 \cdot H_2O$: C, 64.38; H, 6.33; N, 14.65. Found: C, 64.72; H, 6.12; N, 14.62.

EXAMPLE 142

2-((2-Azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-carboxylic acid (142). A solution of sodium hydroxide (30 mg) in 2 mL of water was added to a solution of 356 mg of 2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (0.500 mmol) in 2 mL of dioxane. The resulting mixture was stirred at room temperature for 2 hours. The solvent was removed in vacuo. The residue was dissolved in 10 mL of water and extracted with a 1:1 mixture of ether-hexane (10 mL). The aqueous extract was acidified to pH 4 (concentrated HCl), and the precipitated yellow solid was collected to give 283 mg of the title compound (82%): mp 118 °C (decomp.); Anal. Calc for $C_{38}H_{43}N_7O_6$: C, 65.78; H, 6.26; N, 14.12. Found: C, 65.55; H, 6.31; N, 13.96.

EXAMPLE 143

2-((2-Azidoethyl)oxy)methyl-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (143). A solution of 600 mg of 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-carboxylic acid (0.865 mmol), DCC (357 mg, 1.73 mmol), and DMAP (85 mg, 0.692 mmol) in 15 mL of dry dichloromethane was stirred at room

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temperature for 2 hours. The reaction mixture was charged with 522 mg of concentrated ammonia solution, and the reaction mixture was stirred at room temperature for 3 days. The reaction mixture was filtered, concentrated in vacuo and the crude product was chromatographed (silica, MeOH-EtOAc, 1:9, 1:8, 1:4) to give 528 mg of product as a yellow foamy solid (88%): mp 88-93 °C; Anal. Calc. for $C_{38}H_{44}N_8O_5 \cdot 0.5H_2O$: C, 65.03; H, 6.46; N, 15.97. Found: C, 64.80; H, 5.96; N, 15.88.

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EXAMPLE 144

2-((2-Aminoethyl)oxy)methyl-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (144). A solution of 61 mg of 2-((2-azidoethyl)oxy)methyl-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (0.088 mmol), triphenylphosphine (30 mg, 0.114 mmol), and water (2.5 mg, 0.141 mmol) in 1 mL EtOAc was stirred at room temperature for 3 days. The reaction mixture was concentrated in vacuo, and chromatographed (silica, NH_3 (2N in methanol):MeOH:CHCl₃ (1:2:20)) to give 32 mg of the title compound (55%) as a yellow solid: mp 98-103 °C; Anal. Calcd for $C_{38}H_{46}N_8O_5 \cdot 1.0H_2O \cdot 0.2CH_2Cl_2$: C, 65.38; H, 6.95; N, 11.97. Found: C, 65.39; H, 6.58; N, 11.44.

Using trimethylphosphine as the reducing agent, on a large scale (3 mmol), a 93% yield of the 144 was realized. The product from this batch had the following microanalytical data: Anal. Calc. for $C_{38}H_{46}N_8O_5 \cdot 1.3H_2O$: C, 66.12; H, 7.10; N, 12.18. Found: C, 66.17; H, 6.69; N, 12.09

The enantiomers of 144 were separated on a Chirapak AS (2 x 25 cm) column. The retention times on the semi-prep column were dependent on the column load. At a 60 mg

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load, the retention times were 128 and 228 minutes (hexane-ethanol-isopropanol (containing 3% diethylamine) 84:3:13). The retention times on the analytical Chirapak AS column (4.6 mm x 25 cm), using the same solvent mixture were 34 and 54 minutes (broad peaks). The plus isomer eluted first followed by the minus isomer. The purity of the final selected enantiomeric fractions were >99.9%.

-10: $[\alpha]_{100} = -39.8$

10 +10: $[\alpha]_{100} = +40.1$

EXAMPLE 145

2-((2-Azidoethyl)oxy)methyl-6-methyl-6-ethyl-5-(N-ethyl)
15 carboxamido-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (145).
A solution of 80 mg of 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-
20 carboxylic acid (0.115 mmol), 33 mg of DMAPECD (0.173 mmol), and 31 mg of DMAP in 1 mL of dichloromethane were stirred at room temperature for 2 hours. The reaction mixture was charged with 1.15 mmol of ethylamine (70% solution in water). The reaction mixture was stirred at
25 room temperature for 10 hours and then heated at reflux temperature for 10 hours. The reaction mixture was concentrated in vacuo, dissolved in 3 mL of ethyl acetate, with some drops of dichloromethane added to make the solution homogeneous. The resulting mixture was washed
30 with aqueous saturated NH_4Cl solution (2 X 2 mL), dried (Na_2SO_4), and the solvent removed in vacuo. The crude product was chromatographed (silica, MeOH-EtOAc, 1:9) to give 44 mg of the desired product as a yellow solid (53%): mp 82-87 °C; Anal Calcd. for $\text{C}_{40}\text{H}_{48}\text{N}_8\text{O}_5 \cdot 2.0\text{H}_2\text{O}$: C, 63.47; H, 6.92; N, 14.80. Found: C, 63.49; H, 6.24; N, 14.78.

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EXAMPLE 146

2-((2-Aminoethyl)oxy)methyl-6-ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-
5 (4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (146). A solution of 30 mg of 2-((2-azidoethyl)oxy)methyl-6-ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl)) carboxamidopyridine (0.042 mmol), tri-
10 phenylphosphine (17 mg, 0.063 mmol), and water (1.5 mg, 0.084 mmol) in 3 mL of EtOAc were stirred at room temperature for 19 hrs. Triphenylphosphine (2 mg) and water (1 mg) were added to the reaction mixture and stirred for 24 hrs. The reaction mixture was
15 concentrated in vacuo, and the crude product was chromatographed on silica (NH₃ (2 N in methanol)-MeOH-CHCl₃, 1:2:20) to give 13 mg of product as a yellow solid (45%: mp 115-111 °C; Anal. Calc. for C₄₀H₅₀N₆O₅·1.0H₂O·0.6CH₂Cl₂: C, 63.84; H, 7.02; N, 11.00. Found: C,
20 63.79; H, 6.96; N, 10.81.

EXAMPLE 147

25 2-((2-Azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-3-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitro)phenylpyridine. A solution of 150 mg of 2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-3-carboxylic acid
30 (0.085 mmol), DMAPECD (92 mg, 0.128 mmol), and DMAP (49 mg, 0.102 mmol) in 1.2 mL of dichloromethane was stirred at room temperature for 2.5 hours. The reaction mixture was charged with 27 mg of ethylamine (70% solution in water) and the reaction mixture was heated at reflux
35 temperature for 4 hours. The solvent was removed in vacuo and the crude product was chromatographed (silica, EtOAc-hexane, 3:2) to give 101 mg of the desired product

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as a yellow solid which was used in the next experiment after spectral characterization.

2-((2-Azidoethyl)oxy)methyl-6-ethyl-3-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitro)phenylpyridine-5-carboxylic acid. A solution of 12.5 mg of NaOH in 2 mL of water was added to a solution of 104 mg of 2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-3-(N-ethyl)carboxamido-1,4-dihydro-4-(4-(4-nitro)phenylpyridine (0.21 mmol) in 2 mL of dioxane. The resulting mixture was stirred at room temperature for 2 hours, and the solvent was removed in vacuo. The crude product was partitioned between water (5 mL) and ether (5 mL), separated, acidified (concentrated HCl, pH = 5) and the precipitated oil was extracted with ethyl acetate (2 X 5 mL). The combined organic extracts were dried (Na₂SO₄), and the solvent was removed in vacuo to yield 49 mg of the desired product as a yellow solid: mp 72-77 °C. The product was used in the next step after spectral characterization.

2-((2-Azidoethyl)oxy)methyl-6-ethyl-3-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitro)phenyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (147). A mixture of 40 mg of 6-((2-azidoethyl)oxy)methyl-2-ethyl-3-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitro)phenylpyridine-5-carboxylic acid (0.090 mmol), DMAPECD (26 mg, 0.135 mmol), and DMAP (13 mg, 0.108 mmol) in 2 mL of dry dichloromethane was stirred at room temperature for 3 hours. The reaction mixture was charged with 35 mg of N-3-aminopropyl-4,4-diphenylpiperine, and the resulting mixture was heated at reflux temperature for 17.5 hours. The reaction mixture was diluted with 2 mL of EtOAc, washed with saturated aqueous NH₄Cl solution (2 X 2 mL), dried (Na₂CO₃), and the solvent was removed in vacuo. The crude product was chromatographed (silica, 10% MeOH-EtOAc) to give 30 mg of

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the desired product as a yellow solid (468): mp 83-87 °C; Anal. Calc. for $C_{40}H_{40}N_6O_5 \cdot 3H_2O$: C, 62.00; H, 7.02; N, 14.46. Found: C, 61.84; H, 6.74; N, 14.75.

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EXAMPLE 148

2-((2-azidoethyl)oxy)methyl-6-ethyl-3-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitro)phenyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridino
 10 (148). A solution of 15 mg of 2-((2-azidoethyl)oxy)methyl-6-ethyl-3-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitro)phenyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (0.021 mmol), triphenylphosphine (8.2 mg, 0.031 mmol), and 1.9 mg of
 15 water (0.105 mmol) in 1.5 mL of ethyl acetate were stirred at room temperature for 1 day, 2 mg of triphenylphosphine and 2 mg of water were added to the reaction mixture and stirred for one day, concentrated in vacuo, and the crude product was chromatographed (silica,
 20 NH_3 (2 N in methanol)-MeOH- $CHCl_3$, 1:2:20) to afford 5.1 mg of the desired product as a yellow solid (288): mp 116-120 °C; Anal. Calc. for $C_{40}H_{40}N_6O_5 \cdot 1.0H_2O \cdot 1.0CH_2Cl_2$: C, 61.72; H, 6.82; N, 10.53. Found: C, 61.95; H, 6.74; N, 10.49.

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EXAMPLE 149

2-((2-azidoethyl)oxy)methyl-3-carboxamido-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridino. A solution of 199 mg of 2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-3-carboxylic acid (0.423 mmol), DMAPECD (122 mg, 0.635 mg), and DMAP (41 mg, 0.338 mmol) in 3 mL of dry dichloromethane were
 30 stirred at room temperature 3 hours. The reaction mixture was charged with 530 mg of concentrated ammonia solution and the resulting mixture was heated at reflux

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temperature for 3.5 hrs. The reaction mixture was cooled, filtered and chromatographed (silica, EtOAc-hexane, 1:1, 2:1, 2.5:1) to give 55 mg of spectrally pure product along with 15 mg of slightly impure product for a combined yield of 40%: mp 114-119 °C. The product was used in the next step without any further purification.

2-((2-Azidoethyl)oxy)methyl-3-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-5-carboxylic acid. A solution of 12 mg of NaOH in 0.6 mL of water was added to 60 mg of 2-((2-azidoethyl)oxy)methyl-3-carboxamido-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine (0.127 mmol) in 2 mL of acetone. The resulting mixture was stirred at room temperature for 3.5 hours. The acetone was removed under reduced pressure, acidified with 0.2 N HCl solution, filtered, the residue was dissolved in 5 mL EtOAc, dried (Na₂SO₄) and the solvent was removed in vacuo to yield 46 mg of the desired product (80%): mp 86 °C (decomp.). The product was used in the next step after spectral characterization.

EXAMPLE 149

2-((2-Azidoethyl)oxy)methyl-3-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carbamidopyridine (149). A solution of 40 mg of 2-((2-azidoethyl)oxy)methyl-3-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-5-carboxylic acid (0.096 mmol), DMAPECD (28 mg, 0.143 mmol), and DMAP (9 mg, 0.077 mmol) in 3 mL of dichloromethane was stirred at room temperature for 3 hours. The reaction mixture was charged with 40 mg of N-(3-aminopropyl)-4,4-diphenylpiperidine and the resulting mixture was heated at reflux temperature for 12 hrs. The reaction mixture was diluted with 3 mL of ethyl acetate, washed with aqueous saturated NH₄Cl solution (2 X 5 mL), dried (Na₂CO₃), and the solvent

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was removed in vacuo. The crude product was chromatographed (silica, MeOH-EtOAc, 1:9 to 1:6) to afford 18 mg of spectrally pure product and 40 mg of slightly impure product for a combined yield of 88%: mp 5 87-91 °C; Anal. Calc. for $C_{38}H_{44}N_8O_5 \cdot 0.4H_2O$: C, 65.20; H, 6.45; N, 16.01. Found: C, 65.49; H, 6.65; N, 15.45.

EXAMPLE 150

10 2-((2-Aminoethyl)oxy)methyl-3-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (150). A solution of 40 mg of 2-((2-azidoethyl)oxy)methyl-3-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-5-(N-(3-(4,4-diphen-
15 ylpiperidin-1-yl)propyl)carboxamidopyridine (0.0577 mmol), 45 mg of triphenylphosphine (0.173 mmol), and 10 mg of water in 1.5 mL of ethyl acetate were stirred at room temperature for 13 hrs, and the crude product was chromatographed (silica, NH_3 (2N in methanol)-MeOH- $CHCl_3$,
20 1:2:20) to give 14 mg of the desired product as a yellow solid: mp 116-120 °C; Anal. Calc. for $C_{38}H_{46}N_8O_5 \cdot 1.0H_2O \cdot 1.0CH_2Cl_2$: C, 60.85; H, 6.55; N, 10.92. Found: 60.69; H, 6.51; N, 10.86.

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EXAMPLE 151

2-((2-Azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-3-(N-methyl)carboxamido-4-(4-nitro)phenylpyridine. A mixture of 188 mg of 2-((2-
30 azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-3-carboxylic acid (0.400 mmol), 115 mg of DMAPECD (0.600 mmol), and 58.6 mg of DMAP (0.480 mmol) in 5 mL of dry dichloromethane were stirred at room temperature 2.75 hours. A solution of
35 methylamine in water (40%, 0.40 mL, 4.80 mmol) was added, and the reaction mixture was heated at reflux temperature for 4 hours. The reaction mixture was cooled, solvent

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removed in vacuo, and the residue was chromatographed on 100 g of silica packed with EtOAc-hexane (3:2) to give 55 mg of the desired product as a yellow paste (29%). The product was used in the next step after spectral
5 characterization.

2-((2-Azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(N-methyl)carboxamido-4-(4-nitro)phenylpyridine-5-carboxylic
10 acid. 2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-3-(N-methyl)carboxamido-4-(4-nitro)phenylpyridine (50.0 mg, 0.103 mmol) was dissolved in 0.5 mL of dioxane, NaOH (6.2 mg, 0.155 mmol) in 0.5 mL of water was added to the reaction
15 mixture, and stirred at room temperature for 2.5 hours. The reaction mixture was diluted with 2 mL of ether-hexane (1:1), separated, the aqueous layer was acidified with concentrated HCl (pH = 2-3), extracted with 2 X 2 mL of EtOAc, the combined EtOAc extracts were dried (Na₂SO₄),
20 and the solvent was removed in vacuo to give 44 mg of the desired product as a yellow paste. The product was used in the next step after spectral characterization.

2-((2-Azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(N-methyl)carboxamido-4-(4-nitro)phenyl-5-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (151). A mixture of 44.0 mg of 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(N-methyl)carboxamido-4-(4-nitro)phenylpyridine-5-carboxylic acid (0.100 mmol), 30.0
30 mg of DMAPECD (0.160 mmol), and 15.0 mg of DMAP (0.120 mmol) in 2 mL of dry dichloromethane were stirred at room temperature for 2 hours. The reaction mixture was charged with 34.0 mg of N-(3-aminopropyl)-4,4-diphenylpiperidine, and the resulting mixture was heated
35 at reflux temperature for 6 hours. The reaction mixture was cooled, and the solvent was removed in vacuo. The residue was dissolved in 5 mL of CH₂Cl₂-EtOAc (3:2),

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washed with 2 X 4 mL of aqueous saturated NH_4Cl solution, dried (Na_2CO_3), and the solvent was removed in vacuo. The crude product was chromatographed on 50 g of silica packed with 10% MeOH-EtOAc to give 24.0 mg of the desired product (34%) as a yellow solid.

The hydrochloride salt was prepared by addition of a dichloromethane solution (2 mL) of the free base (24 mg) into 2 mL of 1 N HCl in ether. The precipitated yellow solid was collected to give 20 mg of the desired product: mp 200 °C (decomp.); Anal. Calcd for $\text{C}_{39}\text{H}_{46}\text{N}_8\text{O}_5 \cdot \text{HCl} \cdot 2.4\text{CH}_2\text{Cl}_2$: C, 52.50; H, 5.51; N, 11.83. Found: C, 52.67; H, 5.87; N, 11.66.

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EXAMPLE 152

2-(Trimethylsilyl)ethyl Acetoacetate. A mixture of 6.70 g of 2-trimethylsilylethanol (56.7 mmol) and 8.05 g of 2,2,6-trimethyl-4H-1,3-dioxin-4-one (56.7 mmol) was placed in a round bottom flask equipped with a short distillation apparatus and heated to drive off acetone. The calculated amount of acetone was collected, and the residue was distilled under reduced pressure. The fraction boiling at 106-110 °C (5-10 mmHg) was collected (8.52 g, 74%). The product was used in the next step after spectral characterization.

2-Trimethylsilylethyl 2-(4-nitro)phenylmethyleno-3-oxobutanoate. A mixture of 7.35 g of 2-(trimethylsilyl)ethyl acetoacetate (36.3 mmol), 5.49 g of p-nitrobenzaldehyde (36.3 mmol), 309 mg of piperidine (3.63 mmol), and 218 mg of acetic acid (3.63 mmol) in 100 mL of isopropanol was stirred at room temperature for 16 hours. The solvent was removed in vacuo, and the resulting yellow oil was placed under high vacuum (with occasional heating with a heat gun) until there was no bubbling. The resulting yellow solid was triturated with

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isopropanol, filtered, and washed with isopropanol to give the desired product as a pale yellow crystalline solid (11.0 g, 90%) (a mixture of E/Z isomers): mp 63-65 °C; Anal Calcd for $C_{16}H_{21}N_3SiO_5$: C, 57.29; H, 6.31; N, 4.18. Found: C, 57.20; H, 6.35; N, 4.22.

2-((2-Azidoethyl)oxy)methyl-3-(2-cyanoethoxy)carbonyl)-1,4-dihydro-6-methyl-5-(2-(trimethylsilyloxy)carbonyl)-4-(4-nitro)phenylpyridine. A mixture of 1.31 g of 2-cyanoethyl 4-(2-azidoethoxy)oxy-3-oxobutanoate (5.45 mmol) and 504 mg of ammonium acetate (6.54 mmol) in 5 mL of ethanol (denatured) were heated at reflux temperature for 15 min, cooled, and 1.83 g of 2-(trimethylsilyl)ethyl 2-(4-nitro) phenylmethyleno-3-oxobutanoate (5.45 mmol) was added to the reaction mixture. The resulting mixture was heated at reflux temperature for 1 hour, cooled and the solvent was removed in vacuo. The crude product was chromatographed on 400 g of silica packed with 10% EtOAc-hexane. The column was eluted with 20% (1 L), 30% (2 L), and 40% EtOAc-hexane (3 L) to afford 980 mg of pure (spectra), and 520 mg of slightly impure product for a combined yield of 49% as a yellow oily solid: Anal. calcd for $C_{23}H_{22}N_6SiO_7$: C, 53.94; H, 5.80; N, 15.10. Found: C, 53.80; H, 5.90; N, 15.25.

2-((2-Azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-5-(2-(trimethylsilyloxy)carbonyl)-4-(4-nitro)phenylpyridine-3-carboxylic acid. A solution of 48 mg of NaOH in 1 mL of water was added to 518 mg of 2-((2-azidoethyl)oxy)methyl-3-(2-cyanoethoxy)carbonyl)-1,4-dihydro-6-methyl-5-(2-(trimethylsilyloxy)carbonyl)-4-(4-nitro)phenylpyridine (1.21 mmol) in 5 mL of dioxane. The reaction mixture was stirred at room temperature for 2 hrs, concentrated in vacuo, dissolved in 10 mL of ethyl acetate, washed with 2 X 5 mL of 1 N HCl solution, dried (Na_2SO_4), and the solvent was removed in vacuo. The crude product was recrystallized from a mixture of EtOAc-hexane

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to give 399 mg of the title compound (85%) as a yellow crystalline solid: mp 145-150 °C (decomp.); Anal. Calc. for $C_{22}H_{27}N_7SiO_7$: C, 52.47; H, 5.81; N, 13.91. Found: C, 52.47; H, 5.61; N, 13.87.

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2-((2-Azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-5-(2-trimethylsilyloxy)carbonyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridino (152). A mixture of 190 mg of 2-((2-azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-5-(2-trimethylsilyloxy)carbonyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (0.377 mmol), 117 mg of DCC (0.566 mmol), and 51 mg of DMAP in 5 mL of dry dichloromethane was stirred at room temperature for 1 hour. The reaction mixture was charged with 119 mg of 1-(3-aminopropyl)-4,4-diphenylpiperidine (0.452 mmol) and the resulting mixture was heated at reflux temperature for 2 hours. The reaction mixture was filtered, and chromatographed on 200 g of silica packed with 2.5% MeOH-EtOAc. The column was eluted with 2.5% (0.5 L), 5% (0.5 L), 10% (1 L), and 15% MeOH-EtOAc (1 L) to give 271 mg of product as a yellow foamy solid (92%): mp 63 °C (decomp.); Anal. Calcd for $C_{42}H_{53}N_7SiO_6 \cdot 0.75CH_2Cl_2$: C, 61.25; H, 6.55; N, 11.72. Found: C, 61.69; H, 6.04; N, 12.13.

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EXAMPLE 153

2-((2-Azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridino-5-carboxylic acid (153). A solution of 0.347 mmol of tetrabutylammonium fluoride (1 M in THF) was added to a solution of 246 mg of 2-((2-azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-5-(2-trimethylsilyloxy)carbonyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (0.315 mmol) in 4 mL of dry THF. After 2 hrs, 694 mL of 1 N tetrabutylammonium fluoride was added to the reaction mixture and stirred for 12 hours. The solvent was

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removed in vacuo, and the residue was partitioned between 20 mL of EtOAc and 10 mL of water, separated and washed with 2 X 10 mL of water. The ethyl acetate extract was diluted with 20 mL of hexane and extracted with 3 X 10 mL of 0.5 N NaOH solution. The combined aqueous extracts were acidified with concentrated HCl (pH 2-3) and the separated oily solid was extracted with 2 X 10 mL of dichloromethane. The combined organic extracts were dried (Na_2SO_4) and the solvent was removed in vacuo to give 192 mg of the desired product as a yellow foamy solid (89%): mp 135 °C (decomp.); Anal. Calcd for $\text{C}_{27}\text{H}_{21}\text{N}_7\text{O}_6 \cdot 0.45 \text{CH}_2\text{Cl}_2$: C, 62.65; H, 5.88; N, 13.66. Found: C, 62.92; H, 6.00; N, 13.47.

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EXAMPLE 154

2-((2-Azidoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (154). A mixture of 161 mg of 2-((2-azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-carboxylic acid (0.237 mmol), DCC (73 mg, 0.355 mmol), and DMAP (32 mg, 0.261 mmol) in 2 mL of dry dichloromethane was stirred at room temperature for 1 hour. The reaction mixture was charged with 100 mL of concentrated ammonia and stirred at room temperature for 16 hours. The reaction mixture was filtered, concentrated, dissolved in 5 mL of ethyl acetate, filtered, washed with aqueous saturated ammonium chloride solution (3 X 2 mL), and solvent removed in vacuo. The crude product was chromatographed on 200 g of silica packed with 2 N NH_3 (in methanol)-MeOH- CHCl_3 - CH_2Cl_2 (1:2:20:20). The column was eluted with the above solvent system to give 125 mg of the desired product as a yellow foamy solid (78%): mp 90-95 °C (decomp.); Anal. Calcd for $\text{C}_{37}\text{H}_{32}\text{N}_{10}\text{O}_5 \cdot 0.3 \text{CHCl}_3$: C, 62.69; H, 5.97; N, 15.68. Found: C, 62.53; H, 5.32; N, 15.12.

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EXAMPLE 155

2-((2-Aminoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (155). A solution of 85 mg of 2-((2-azidoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (0.125 mmol), 49.3 mg of triphenylphosphine (0.188 mmol), and 7 mL of water in 2 mL of THF were stirred at room temperature for 2 days. TLC showed small amounts of the starting material in the reaction mixture. Triphenylphosphine (5 mg) was added to the reaction mixture and stirred for 1 day. The solvent was removed in vacuo, and the crude product was chromatographed on 120 g of silica packed with NH_3 (2 M in MeOH):MeOH: CHCl_3 (1:2:17). The column was eluted with 1:2:17, 1:2:15, and 1:2:10 (NH_3 (2 M in MeOH):MeOH: CHCl_3) to give 20 mg of the desired product. The chromatographed product was dissolved in 5 mL of CH_2Cl_2 and 5 mL of saturated sodium carbonate mixture, separated, dried over Na_2SO_4 , and the solvent was removed in vacuo. The residue was triturated with CH_2Cl_2 -ether (1:2) to give a yellow solid: Anal. calc. for $\text{C}_{37}\text{H}_{44}\text{N}_6\text{O}_5 \cdot 1.4\text{CHCl}_3 \cdot 1.4\text{H}_2\text{O}$: C, 54.57; H, 5.75. Found: C, 54.50; H, 5.81

EXAMPLE 152

1,4-Dihydro-3-(N-isopropyl)carboxamido-2,6-dimethyl-4-(4-nitrophenyl)-5-(N-[3-(4,4-diphenylpiperidin-1-yl)propyl])carboxamidopyridine (156). A suspension of 4-nitrobenzaldehyde (10.00 g, 66.2 mol), 2-cyanoethyl acetoacetate (10.27 g, 66.2 mol), piperidine (281 mg, 3.31 mmol) and acetic acid (198 mg, 3.31 mmol) in 250 mL of 2-propanol was stirred at room temperature for 48 hrs. Reaction mixture was filtered, the solid collected and dried in air to give 2-[(4-nitrophenyl)methylene]-3-

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oxobutanoic acid 2-cyanoethyl ester as a white powder (11.24 g, 59%).

A solution of 2-[(4-nitrophenyl)methylene]-3-oxobutanoic
5 acid 2-cyanoethyl ester (15.06 g, 52.3 mmol) and benzyl
3-amino-crotonate (10.00 g, 52.3 mmol) in 150 ml of EtOH
was refluxed for 36 hrs. After solvent was evaporated,
the residue was dissolved in 250 ml of CHCl_3 , washed with
water (2x100 ml) and dried over Na_2SO_4 . After filtration
10 and evaporation of solvent, 3-benzyloxycarbonyl-5-(2-
cyanoethoxy)carbonyl-1,4-dihydro-2,6-dimethyl-4-(4-
nitrophenyl)pyridine was obtained as a yellow oil (23.4
g, 97%).

15 A solution of 3-benzyloxycarbonyl-5-(2-
cyanoethoxy)carbonyl-1,4-dihydro-2,6-dimethyl-4-(4-
nitrophenyl)pyridine (3.24 g, 7.02 mmol) in 160 ml of
4.4% (w/w) formic acid/MeOH mixture was stirred with Pd/C
(10%, 3.24 g) for 30 min., the reaction was quenched by
20 addition of 10 ml of CHCl_3 . The mixture was filtered and
concentrated to give a yellow powder, which was dissolved
in CHCl_3 (100 ml), washed with water (25 ml) and aqueous
1N HCl (25 ml). After drying (Na_2SO_4) and evaporation of
solvent, 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-2,6-
25 dimethyl-4-(4-nitrophenyl)pyridine-5-carboxylic acid was
obtained as a yellow powder (1.94 g, 75%).

A solution of 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-2,6-
dimethyl-4-(4-nitrophenyl)pyridine-5-carboxylic acid (473
30 mg, 1.35 mmol), 1-(3-dimethylaminopropyl)-3-
ethylcarbodiimide hydrochloride (532 mg, 2.69 mmol) and
4-dimethylaminopyridine (164 mg, 1.35 mmol) in 50 ml of
 CH_2Cl_2 was stirred at room temperature. After 1 hr, a
solution of isopropylamine (398 mg, 6.73 mmol) in 2 ml of
35 CH_2Cl_2 was added and the mixture was stirred at room
temperature overnight. The mixture was washed with water
(30 ml), saturated aqueous NH_4Cl (3x25 ml), 10% aqueous

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K_2CO_3 (25 ml) and brine (30 ml). After dried over Na_2SO_4 and removal of solvent in vacuo, 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-5-(N-isopropyl)carboxamido-2,6-dimethyl-4-(4-nitrophenyl)pyridine was obtained as a yellowish powder (524 mg, 94%).

A solution of 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-5-(N-isopropyl)carboxamido-2,6-dimethyl-4-(4-nitrophenyl)pyridine (500 mg, 1.20 mmol) in 10 ml of acetone was treated with 5 ml of 1N aqueous KOH solution at 0°C for 45 min. The acetone was removed in vacuo and the aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the resulting yellow precipitate was collected by filtration, washed with 5 ml of cold water and dried in vacuo to yield 1,4-dihydro-5-(N-isopropyl)carboxamido-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid as a yellow powder (244 mg, 56%).

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A solution of 1,4-dihydro-5-(N-isopropyl)carboxamido-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (240 mg, 0.67 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (250 mg, 1.34 mmol) and 4-dimethylaminopyridine (80 mg, 0.67 mmol) in 20 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (190 mg, 0.67 mmol) in 2 ml of CH_2Cl_2 was added and the mixture was stirred at reflux overnight. The mixture was washed with water (10 ml), saturated aqueous NH_4Cl (3×10 ml), 10% aqueous K_2CO_3 (10 ml) and brine (10 ml). After dried over Na_2SO_4 and removal of solvent in vacuo, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , MeOH: $CHCl_3$:1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. 1,4-Dihydro-3-(N-isopropyl)carboxamido-2,6-dimethyl-4-(4-nitrophenyl)-5-{N-[3-(4,4-diphenylpiperidin-1-

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yl)propyl}}carboxamidopyridine was obtained as a yellowish powder (263 mg, 62%). M.p. 123-125 °C; Calcd. for $C_{38}H_{45}N_5O_4$: C 71.78, H 7.13, N 11.02; Found: C 71.52, H 7.13, N 10.99.

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EXAMPLE 157

6-Ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl}}carboxamido-2-propylpyridine (157). In a round-bottomed flask equipped with a distillation apparatus, a mixture of ethyl butyrylacetate (50.0 g, 0.316 mol) and 3-hydroxypropionitrile (67.4 g, 0.948 mol) was heated in a oil bath at 190 °C. After most of the EtOH was distilled over, the mixture was vacuum distilled and 2-cyanoethyl butyrylacetate was collected at 125-135 °C/0.1 mmHg (26.0 g, 44.9 %).

A suspension of 4-nitrobenzaldehyde (16.61 g, 110 mmol), 2-cyanoethyl butyrylacetate (19.34 g, 100 mmol), piperidine (430 mg, 5.00 mmol) and acetic acid (300 mg, 5.00 mmol) in 350 ml of 2-propanol was stirred at room temperature for 48 hrs. The reaction mixture was filtered and resulting solid was air dried to give 2-[(4-nitrophenyl)methylene]-3-oxohexanoic acid 2-cyanoethyl ester as a white powder (31.0 g, 95%).

A solution of 2-[(4-nitrophenyl)methylene]-3-oxohexanoic acid 2-cyanoethyl ester (16.3 g, 50 mmol) and benzyl 3-amino-2-pentenoate (11.3 g, 55 mmol) in 250 ml of EtOH was refluxed for 36 hrs. After the solvent was removed in vacuo, the residue was dissolved in 250 ml of $CHCl_3$, washed with water (2x100 ml) and dried over Na_2SO_4 . After filtration and evaporation of solvent, 3-benzyloxycarbonyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-2-propylpyridine was obtained as a yellow oil (25.1 g, 98%).

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A solution of 3-benzyloxycarbonyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-2-propylpyridine (5.00 g, 10.0 mmol) in 150 ml of 4.4%(w/w) formic acid/MeOH mixture was stirred with
5 Pd/C (10%, 2.50 g) at room temperature. After 40 min., the reaction was quenched by addition of 50 ml of CHCl_3 . The mixture was filtered and concentrated in vacuo to yield a yellow powder, which was dissolved in CHCl_3 (150 ml), washed with 0.5N aqueous HCl (50 ml) and brine (50
10 ml), then dried over Na_2SO_4 . After filtration and evaporation of solvent, 3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-2-propylpyridine-5-carboxylic acid was obtained as a yellow powder (3.80 g, 93%).

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A solution of 3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-2-propylpyridine-5-carboxylic acid (2.50 g, 6.00 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.30 g, 12.0 mmol) and
20 4-dimethylaminopyridine (0.74 g, 6.00 mmol) in 200 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, 4.5 ml of ethylamine (70% aqueous solution) was added to the solution and the mixture was stirred at room temperature overnight. The mixture was washed with water (200 ml),
25 saturated aqueous NH_4Cl (3x200 ml), 10% aqueous K_2CO_3 (200 ml) and brine (200 ml). After dried over Na_2SO_4 and evaporation of solvent, 3-(2-cyanoethoxy)carbonyl-6-ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2-propylpyridine was obtained as a yellowish
30 powder (2.45 g, 92%).

A solution of 3-(2-cyanoethoxy)carbonyl-6-ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2-propylpyridine (2.40 g, 5.50 mmol) in 50 ml acetone was
35 treated with 20 ml 1N aqueous KOH solution at 0°C for 1 hr. The acetone was removed in vacuo and the aqueous layer was washed with CHCl_3 (40 ml) then acidified to pH=3

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by 2N hydrochloric acid. The resulting yellow precipitate was collected by filtration, washed with 5 ml of cold water and dried in vacuo to yield 6-ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2-propylpyridine-3-carboxylic acid as a yellow powder (1.72 g, 82%)

A solution of 6-ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2-propylpyridine-3-carboxylic acid (1.50 g, 3.87 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.48 g, 7.74 mmol) and 4-dimethylaminopyridine (670 mg, 5.10 mmol) in 50 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (1.14 g, 3.87 mmol) in 5 ml of CH_2Cl_2 was added and the mixture was stirred at reflux overnight. The mixture was washed with water (20 ml), saturated aqueous NH_4Cl (3x20 ml), 10% K_2CO_3 (20 ml) and brine (20 ml). After dried over Na_2SO_4 and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. 6-Ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamido-2-propylpyridine was obtained as a yellowish powder (1.65 g, 64%). M.p. 201 °C (dec.); Calcd. for $\text{C}_{40}\text{H}_{49}\text{N}_5\text{O}_4 \cdot 1/2\text{H}_2\text{O}$: C 71.40, H 7.49, N 10.41; Found: C 71.23, H 7.23, N 10.42.

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EXAMPLE 158

6-Ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2-pentyl-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (158). To a solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (43.2 g, 300 mmol) and pyridine (47.5 g, 600 mmol) in 300 ml of CH_2Cl_2 was added hexanoyl chloride (40.4 g, 300 mmol) dropwise at 0 °C.

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The mixture was stirred at 0 °C for 1 hr then at room temperature for 1 hr. The solution was washed with 1N aqueous HCl (300 ml), water (300 ml) and dried over Na₂SO₄. After evaporation of solvent, 5-hexanoyl-2,2-dimethyl-1,3-dioxane-4,6-dione was obtained as a light pink oil (35.4 g, 62%).

5-Hexanoyl-2,2-dimethyl-1,3-dioxane-4,6-dione (35.4 g, 146 mmol) was heated with 3-hydroxypropionitrile (40.0 g, 560 mmol) at 120 °C until no more CO₂ was released. The mixture was vacuum distilled and 2-cyanoethyl hexanoylacetate was collected at 128-145 °C/0.2 mmHg (21.3 g, 69%).

A mixture of 2-cyanoethyl hexanoylacetate (21.1 g, 100 mmol), 4-nitrobenzaldehyde (16.6 g, 110 mmol), piperidine (430 mg, 5.00 mmol) and acetic acid (300 mg, 5.00 mmol) in 350 ml of 2-propanol was stirred at room temperature for 48 hrs. The resulting white precipitate was filtered and dried in the air. The product, 2-[(4-nitrophenyl)methylene]-3-oxooctanoic acid 2-cyanoethyl ester was obtained as a white powder (25.2 g, 73% yield).

A solution of 2-[(4-nitrophenyl)methylene]-3-oxooctanoic acid 2-cyanoethyl ester (6.89 g, 20 mmol) and benzyl 3-amino-2-pentenoate (4.52 g, 22 mmol) in 300 ml of EtOH was refluxed for 36 hrs. After the solvent was removed in vacuo, the residue was dissolved in 250 ml of CHCl₃, washed with water (2×100 ml) and dried over Na₂SO₄. After filtration and evaporation of solvent, 3-benzyloxycarbonyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-2-pentylpyridine was obtained as a yellow oil (10.5 g, 99%).

A solution of 3-benzyloxycarbonyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-2-pentylpyridine (10.5 g, 20.0 mmol) in 200

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ml of 4.4%(w/w) formic acid/MeOH mixture was stirred with Pd/C (10%, 3.15 g) at room temperature. After 80 min., the reaction was quenched by addition of 50 ml of CHCl_3 . The mixture was filtered and concentrated in vacuo to give a yellow powder, which was dissolved in CHCl_3 (250 ml), washed with 0.5N aqueous HCl (100 ml) and brine (100 ML), then dried over Na_2SO_4 . After filtration and evaporation of solvent, 3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-2-pentylpyridine-5-carboxylic acid was obtained as a yellow powder (7.88 g, 82%).

A solution of 3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-2-pentylpyridine-5-carboxylic acid (3.15 g, 6.60 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.50 g, 13.2 mmol) and 4-dimethylaminopyridine (1.2 g, 10 mmol) in 200 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, 2.66 ml of ethylamine (70% aqueous solution) was added and the mixture was stirred at room temperature overnight. The mixture was washed with water (200 ml), saturated aqueous NH_4Cl (3x200 ml), 10% aqueous K_2CO_3 (200 ml) and brine (200 ml). After dried over Na_2SO_4 and evaporation of solvent, 3-(2-cyanoethoxy)carbonyl-6-ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2-pentylpyridine was obtained as a yellowish powder (3.42 g, 100%).

A solution of 3-(2-cyanoethoxy)carbonyl-6-ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2-pentylpyridine (3.30 g, 6.85 mmol) in 40 ml of acetone was treated with 25 ml 1N aqueous KOH solution at 0°C for 1 hr. The acetone was removed in vacuo and the aqueous layer was washed with CHCl_3 (40 ml) then acidified to pH=3 by 2N hydrochloric acid. The resulting yellow precipitate was collected by filtration, washed with 5 ml of cold water and dried in vacuo to yield 6-ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2-

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pentylpyridine-3-carboxylic acid as a yellow powder (3.00 g, 97%)

A solution of 6-ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2-pentylpyridine-3-carboxylic acid (1.58 g, 3.50 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.00 g, 5.25 mmol) and 4-dimethylaminopyridine (450 mg, 3.50 mmol) in 100 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (1.03 g, 3.50 mmol) in 10 ml of CH_2Cl_2 was added and the mixture was stirred at reflux overnight. The mixture was washed with water (50 ml), saturated aqueous NH_4Cl (3x50 ml), 10% aqueous K_2CO_3 (50 ml) and brine (50 ml). After dried over Na_2SO_4 and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. 6-Ethyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2-pentyl-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (1.21 g, 50%). M.p. 115-120 °C; Calcd. for $\text{C}_{42}\text{H}_{53}\text{N}_5\text{O}_4 \cdot 1/2\text{H}_2\text{O}$: C 71.97, H 7.77, N 9.99; Found: C 71.99, H 7.77, N 9.86.

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EXAMPLE 159

5-(N-Ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamido-2,6-dipropylpyridine (159). In a round-bottomed flask equipped with a distillation apparatus, a mixture of ethyl butyrylacetate (31.6 g, 0.20 mol) and benzyl alcohol (23.8 g, 0.220 mol) was heated with an oil bath at 190 °C. After most of the EtOH was distilled over, the mixture was vacuum distilled and benzyl butyrylacetate was collected at 130-136 °C/0.2 mmHg (33.5 g, 76.1 %).

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A mixture of benzyl butyrylacetate (22.0 g, 0.10 mol) and 10 g of 4 Å molecular sieves was treated with ammonia gas which was bubbled through the mixture for 38 hrs at 50 °C. After filtration, benzyl 3-amino-2-hexenoate was
5 obtained as a yellowish oil (21 g, 95%).

A solution of 2-[(4-nitrophenyl)methylene]-3-oxohexanoic acid 2-cyanoethyl ester (9.80 g, 30 mmol) and benzyl 3-amino-2-hexenoate (7.24 g, 33 mmol) in 150 ml of EtOH was
10 refluxed for 36 hrs. After the solvent was removed in vacuo, the residue was dissolved in 250 ml of CHCl₃, washed with water (2×100 ml) and dried over Na₂SO₄. After filtration and evaporation of solvent, 5-benzyloxycarbonyl-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-
15 4-(4-nitrophenyl)-2,6-dipropylpyridine was obtained as a yellow oil (15.4 g, 97%).

A solution of 5-benzyloxycarbonyl-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-4-(4-nitrophenyl)-2,6-dipropylpyridine (10.6 g, 20.4 mmol) in 200 ml of
20 4.4%(w/w) formic acid/MeOH mixture was stirred with Pd/C (10%, 3.50 g) at room temperature. After 1 hr, the reaction was quenched by addition of 50 ml of CHCl₃. The mixture was filtered and concentrated to give a yellow
25 powder, which was dissolved in CHCl₃ (250 ml), washed with 0.5N aqueous HCl (100 ml) and brine (100 ml), then dried over Na₂SO₄. After filtration and evaporation of solvent, 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-4-(4-nitrophenyl)-2,6-dipropylpyridine-5-carboxylic acid was obtained as a
30 yellow powder (8.04 g, 92%).

A solution of 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-4-(4-nitrophenyl)-2,6-dipropylpyridine-5-carboxylic acid (4.28 g, 10.0 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (3.81 g, 20.0 mmol) and
35 4-dimethylaminopyridine (1.6 g, 13 mmol) in 200 ml of CH₂Cl₂ was stirred at room temperature. After 1 hr, 3.20

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g of ethylamine (70% aqueous solution) was added and the mixture was stirred at room temperature overnight. The mixture was washed with water (200 ml), saturated aqueous NH_4Cl (3×200 ml), 10% aqueous K_2CO_3 (200 ml) and brine (200 ml). After dried over Na_2SO_4 and evaporation of solvent, 3-(2-cyanoethoxy)carbonyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2,6-dipropylpyridine was obtained as a yellowish powder (4.15 g, 99%).

10 A solution of 3-(2-cyanoethoxy)carbonyl-5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2,6-dipropylpyridine (4.55 g, 10.0 mmol) in 50 ml of acetone was treated with 40 ml 1N aqueous KOH solution at 0°C for 1 hr. The acetone was removed in vacuo and the aqueous
15 layer was washed with CHCl_3 (40 ml) then acidified to pH=3 by 2N hydrochloric acid, the resulting yellow precipitate was collected by filtration, washed with 5 ml of cold water and dried in vacuo to yield 5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2,6-dipropylpyridine-3-
20 carboxylic acid as a yellow powder (4.00 g, 100%)

A solution of 5-(N-ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-2,6-dipropylpyridine-3-carboxylic acid (1.61 g, 4.00 mmol), 1-(3-dimethylaminopropyl)-3-
25 ethylcarbodiimide hydrochloride (1.15 g, 6.00 mmol) and 4-dimethylaminopyridine (500 mg, 4.00 mmol) in 150 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (1.18 g, 4.00 mmol) in 10 ml of CH_2Cl_2 was added and the
30 mixture was stirred at reflux overnight. The mixture was washed with water (50 ml), saturated aqueous NH_4Cl (3×50 ml), 10% aqueous K_2CO_3 (50 ml) and brine (50 ml). After dried over Na_2SO_4 and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography
35 (SiO_2 , MeOH: CHCl_3 :1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. 5-(N-Ethyl)carboxamido-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-

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1-yl)propyl}}carboxamido-2,6-dipropylpyridine was obtained as a yellowish powder (1.85 g, 68%). M.p. 123-128 °C; Calcd. for $C_{24}H_{31}N_5O_4 \cdot H_2O$: C 70.76, H 7.68, N 10.06; Found: C 70.94, H 7.56, N 10.09.

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EXAMPLE 160

5-(2-Cyanoethoxycarbonyl)-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl}}carboxamidopyridine (160). A mixture of 2-cyanoethyl 3-aminocrotonate (247 mg, 1.60 mmol), 4-nitrobenzaldehyde (242 mg, 1.60 mmol) and N-[3-(4,4-diphenylpiperidin-1-yl)propyl]acetoacetamide (607 mg, 1.60 mmol) in 50 ml of 2-propanol was refluxed for 48 hrs. After the solvent was removed in vacuo, the residue was dissolved in 50 ml of $CHCl_3$, washed with water (25 ml) and dried over Na_2SO_4 . After filtration and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , MeOH: $CHCl_3$:1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. The title compound was obtained as a yellowish powder (267 mg, 26%). M.p. 93-95 °C; Calcd. for $C_{38}H_{41}N_5O_4 \cdot 1/4H_2O$: C 69.97, H 6.41, N 10.74; Found: C 69.73, H 6.22, N 10.66.

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EXAMPLE 161

1,4-Dihydro-4-(4-nitrophenyl)-5-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl}}carboxamido-2,6-dipropylpyridine-3-carboxylic acid (161). A solution of 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-4-(4-nitrophenyl)-2,6-dipropylpyridine-5-carboxylic acid (1.50 g, 3.60 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.38 g, 7.20 mmol) and 4-dimethylaminopyridine (0.45 g, 3.6 mmol) in 150 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine

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(1.06 g, 3.60 mmol) in 10 ml of CH_2Cl_2 was added and the mixture was stirred at room temperature overnight. The mixture was washed with water (100 ml), saturated aqueous NH_4Cl (3x100 ml), 100 ml of 10% aqueous K_2CO_3 and 100 ml
5 of brine. After drying over Na_2SO_4 and evaporation of solvent, 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-4-(4-nitrophenyl)-5-{N-3-[(4,4-diphenylpiperidin-1-yl)propyl]}carboxamido-2,6-dipropylpyridine was obtained as a yellowish powder (640 mg, 26%).

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A solution of 3-(2-cyanoethoxy)carbonyl-1,4-dihydro-4-(4-nitrophenyl)-5-{N-3-[(4,4-diphenylpiperidin-1-yl)propyl]}carboxamido-2,6-dipropylpyridine (640 mg, 0.92 mmol) in 30 ml acetone was treated with 4.6 ml 1N KOH
15 solution at 0°C for 1 hr. The acetone was removed in vacuo and the aqueous layer was washed with CHCl_3 (10 ml) then acidified to pH=3 by 2N hydrochloric acid. The resulting yellow precipitate was collected by filtration, washed with 5 ml of cold water and dried in vacuo. 1,4-
20 Dihydro-4-(4-nitrophenyl)-5-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamido-2,6-dipropylpyridine-3-carboxylic acid was obtained as a yellow powder (485 mg, 81%). M.p. 126-130 °C; Calcd. for $\text{C}_{39}\text{H}_{46}\text{N}_4\text{O}_5 \cdot 2\text{H}_2\text{O}$: C 68.20, H 7.34, N 8.16; Found: C 68.30, H 7.01, N 8.16.

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EXAMPLE 162

1,4-Dihydro-3-{N-[3-(4-hydroxy-4-phenylpiperidin-1-yl)propyl]}carboxamido-2,6-dimethyl-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (162). A
30 solution of 1,4-dihydro-2,6-dimethyl-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (212 mg, 0.64 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (253 mg, 1.28 mmol) and
35 4-dimethylaminopyridine (78 mg, 0.64 mmol) in 30 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4-hydroxy-4-phenylpiperidin-1-

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yl)propylamine (150 mg, 0.64 mmol) in 5 ml of DMF was added and the mixture was stirred at reflux overnight. After cooling to room temperature, the mixture was poured into 150 ml of hexane and a yellowish sticky oil was separated out. The oil was purified by chromatography (SiO₂, MeOH: CHCl₃:1N NH₃ in MeOH, 6:90:3) and precipitated by CH₂Cl₂/hexane mixture. The title compound was obtained as a yellowish powder (20 mg, 5.7%). M.p. 87-91 °C; Calcd. for C₃₀H₃₇N₅O₅: C 65.80, H 6.81, N 12.79; Found: C 66.06, H 6.90, N 12.59.

EXAMPLE 163

4-(3,4-Ethylenedioxyphenyl)-1,4-Dihydro-2,6-dimethyl-5-(N-methyl)carboxamido-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (163). A mixture of 2-cyanoethyl acetoacetate (5.00 g, 32.2 mmol), 1,4-benzodioxan-6-carboxaldehyde (5.29 g, 32.2 mmol), piperidine (137 mg, 1.61 mmol) and acetic acid (97 mg, 1.6 mmol) in 70 ml of 2-propanol was stirred at r.t. for 48 hrs. After evaporation of solvent, the product was purified by chromatography (SiO₂, AcOEt: Hexane, 60:10). 2-[(3,4-Ethylenedioxyphenyl)methylene]-3-oxobutanoic acid 2-cyanoethyl ester was obtained as a yellowish oil (2.64 g, 27% yield).

A solution of 2-[(3,4-ethylenedioxyphenyl)methylene]-3-oxobutanoic acid 2-cyanoethyl ester (2.64 g, 8.76 mmol) and N-methyl 3-amino-2-pentenamide (1.00 g, 8.76 mmol) in 50 ml of EtOH was refluxed for 36 hrs. After solvent was removed in vacuo, the residue was dissolved in 50 ml of CHCl₃, washed with water (2×100 ml) and dried over Na₂SO₄. After filtration and evaporation of solvent, the product was purified by chromatography (SiO₂, CHCl₃:MeOH, 90:10). 3-(2-Cyanoethoxy)carbonyl-4-(3,4-ethylenedioxyphenyl)-1,4-dihydro-2,6-dimethyl-5-(N-methyl)carboxamidopyridine was obtained as a yellow oil (2.15 g, 62%).

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The solution of 3-(2-cyanoethoxy)carbonyl-4-(3,4-ethylenedioxyphenyl)-1,4-dihydro-2,6-dimethyl-5-(N-methyl)carboxamidopyridine (2.15 g, 5.40 mmol) in 30 ml acetone was treated with 30 ml 1N KOH solution at 0 °C for 1 hr. The acetone was removed in vacuo and aqueous layer was washed with CHCl₃ (40 ml) then acidified to pH=3 by 2N hydrochloric acid, the yellow precipitate was collected by filtration, washed with 5 ml of cold water and dried in vacuo. 4-(3,4-Ethylenedioxyphenyl)-1,4-dihydro-2,6-dimethyl-5-(N-methyl)carboxamidopyridine-3-carboxylic acid was obtained as a yellow powder (1.00 g, 54%).

A solution of 4-(3,4-ethylenedioxyphenyl)-1,4-dihydro-2,6-dimethyl-5-(N-methyl)carboxamidopyridine-3-carboxylic acid (250 mg, 0.73 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (287 mg, 1.45 mmol) and 4-dimethylaminopyridine (89 mg, 0.73 mmol) in 50 ml of CH₂Cl₂ was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (170 mg, 0.73 mmol) in 5 ml of CH₂Cl₂ was added and the mixture was stirred at reflux overnight. The mixture was washed with water (20 ml), saturated aqueous NH₄Cl (3x20 ml), 20 ml 10% K₂CO₃ and 20 ml of brine. After drying over Na₂SO₄ and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO₂, MeOH: CHCl₃:1N NH₃ in MeOH, 6:90:3) and precipitated by CH₂Cl₂/hexane mixture. 4-(3,4-Ethylenedioxyphenyl)-1,4-Dihydro-2,6-dimethyl-5-(N-methyl)carboxamido-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (136 mg, 30%). M.p. 115-116 °C; Calcd. for C₃₈H₄₄N₄O₄•3/4H₂O: C 71.96, H 7.23, N 8.83; Found: C 71.81, H 7.09, N 9.10.

EXAMPLE 164

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4-(3,4-Ethylenedioxyphenyl)-1,4-Dihydro-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-

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yl)propyl}}carboxamido-2,6-dimethyl-5-[(N-methyl)carboxamido]pyridine (164). A solution of 4-(3,4-ethylenedioxyphenyl)-1,4-dihydro-2,6-dimethyl-5-[(N-methyl)carboxamido]pyridine-3-carboxylic acid (100 mg, 0.30 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (115 mg, 0.60 mmol) and 4-dimethylaminopyridine (73 mg, 0.60 mmol) in 30 ml of CH₂Cl₂ was stirred at room temperature. After 1 hr, a solution of 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (83.0 mg, 0.30 mmol) in 2 ml of CH₂Cl₂ was added and the mixture was stirred at reflux overnight. The mixture was washed with water (10 ml), saturated aqueous NH₄Cl (3×10 ml), 10 ml 10% K₂CO₃ and 10 ml of brine. After drying over Na₂SO₄ and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO₂, MeOH: CHCl₃:1N NH₃ in MeOH, 6:90:3) and precipitated by CH₂Cl₂/hexane mixture. The title compound was obtained as a yellowish powder (65 mg, 36%). M.p. 101-104 °C; Calcd. for C₃₄H₄₂N₄O₆·5/4H₂O: C 65.31, H 7.17, N 8.96; Found: C 65.12, H 6.69, N 8.69.

EXAMPLE 165

2-(4-Azidobutyl)-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl}}carboxamido-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine (165). A solution of methyl 5-bromovalerate (5.00 g, 25.6 mmol), NaN₃ (3.33 g, 51.2 mmol) and 15 ml of water in 40 ml of MeOH was refluxed for 3.5 hrs. The MeOH was removed in vacuo and residue was partitioned between CHCl₃ (200 ml) and water (50 ml). The organic layer was separated and washed with water. After drying and removal of solvent, methyl 5-azidovalerate (4.01 g, 99.7%) was obtained as a colorless oil.

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Methyl 5-azidovalerate (4.01 g, 25.5 mmol) and KOH (7.58 g, 0.135 mol) were dissolved in a mixture of 70 ml of

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water and 90 ml of MeOH. The solution was stirred at 0 °C. After 2 hrs, the MeOH was removed in vacuo. The aqueous layer was extracted by CHCl₃ (50 ml), acidified to pH=1 by 2N aqueous HCl and extracted by Et₂O (2×100 ml).

5 The organic layers were combined, washed with water (100 ml) and dried over Na₂SO₄. After filtration and evaporation of solvent, 5-azidovaleric acid (2.85 g, 77.6%) was obtained as a colorless oil.

10 5-Azidovaleric acid (2.00 g, 13.9 mmol) in 15 ml of toluene was treated with oxalyl chloride (3.55 g, 27.9 mmol). The mixture was stirred at 50 °C for 10 hrs. After removal of toluene in vacuo, crude 5-azidovaleric chloride was used for next reaction without further
15 purifications.

To the solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (4.45 g, 30.9 mmol) and 4-dimethylaminopyridine (7.55 g, 61.8 mmol) in 100 ml of CH₂Cl₂ was added the solution of
20 crude 5-azidovaleric chloride in 10 ml of CH₂Cl₂ at 0 °C. The mixture was stirred at 0 °C for 1 hr and at room temperature for 1 hr. The solution was washed with 1N aqueous HCl (100 ml), brine (250 ml) and dried over Na₂SO₄. After evaporation of solvent, 5-(5-
25 azidopentanoyl)-2,2-dimethyl-1,3-dioxane-4,6-dione was obtained as a light pink oil (8.17 g, 98%).

5-(5-Azidopentanoyl)-2,2-dimethyl-1,3-dioxane-4,6-dione was heated with 3-hydroxypropionitrile (2.42 g, 34.0
30 mmol) at 80 °C until no more CO₂ was released. After cooling to room temperature, the mixture was diluted with 150 ml of 2-propanol, and 4-nitrobenzaldehyde (4.60 g, 30.3 mmol), piperidine (130 mg, 1.50 mmol) and acetic acid (90 mg, 1.50 mmol) were added. The mixture was
35 stirred at room temperature for 48 hrs. The product, 7-azido-2-[(4-nitrophenyl)methylene]-3-oxoheptanoic acid 2-cyanoethyl ester was obtained as a pale-yellow oil (5.73

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g, 51% yield) after chromatography (SiO_2 , Hexane: AcOEt, 2:1).

A solution of 7-azido-2-[(4-nitrophenyl)methylene]-3-oxoheptanoic acid 2-cyanoethyl ester (3.71 g, 10.0 mmol) and 3-amino-2-pentenamide (1.14 g, 10.0 mmol; this compound was prepared by bubbling ammonia gas through a solution of 6-ethyl-4H-2,2-dimethyl-1,3-dioxin-4-one in xylene at 115 °C for 2 hrs) in 50 EtOH was refluxed for 48 hrs. After the EtOH was removed in vacuo, the residue was dissolved in 150 ml of CHCl_3 , washed with water (2×100 ml) and dried over Na_2SO_4 . After filtration and evaporation of solvent, the product was purified by chromatography (SiO_2 , CHCl_3 :MeOH=5:95). 2-(4-azidobutyl)-5-carboxamido-3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine was obtained as a yellow powder (2.50 g, 54% yield).

A solution of 2-(4-azidobutyl)-5-carboxamido-3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine (1.50 g, 3.20 mmol) in 10 ml acetone was treated with 20 ml 1N aqueous KOH solution at 0°C for 45 min. The acetone was removed in vacuo and the aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the yellow precipitate was collected by filtration, washed with 10 ml of cold water and dried in vacuo. 1.20 g (90% yield) of 2-(4-azidobutyl)-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid was obtained as a yellow powder.

A solution of 2-(4-azidobutyl)-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (300 mg, 0.72 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (276 mg, 1.44 mmol) and 4-dimethylaminopyridine (176 mg, 1.44 mmol) in 50 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4-methoxycarbonyl-4-phenyl)piperidin-1-

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yl)propylamine (215 mg, 0.86 mmol) in 5 ml of CH_2Cl_2 was added and the mixture was stirred at reflux overnight. The mixture was washed with water (30 ml), saturated aqueous NH_4Cl (3x30 ml), 30 ml 10% K_2CO_3 and 30 ml of
5 brine. After drying over Na_2SO_4 and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. 2-(4-Azidobutyl)-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-
10 1-yl)propyl]}carboxamido-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine was obtained as a yellowish powder (320 mg, 66%). M.p. 74-77 °C; Calcd. for $\text{C}_{35}\text{H}_{44}\text{N}_8\text{O}_6$: C 62.48, H 6.59, N 16.66; Found: C 62.27, H 6.30, N 16.62.

15

EXAMPLE 166

2-(4-Aminobutyl)-5-carboxamido-6-ethyl-1,4-dihydro-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-
20 yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (166). A solution of 2-(4-azidobutyl)-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine (280 mg, 0.42 mmol) in 5 ml of
25 AcOEt was treated with 1.25 ml of 1M trimethylphosphine THF solution. The mixture was stirred at 0 °C for 1.5 hrs, 0.22 ml of water was then added and the mixture was stirred at room temperature for an additional 1.5 hrs. After most volatile materials were removed in vacuo,
30 residue was dissolved into AcOEt (50 ml), washed with 6N aqueous KOH (50 ml), brine (50 ml) and dried over K_2CO_3 . After filtration and evaporation of solvent, product was precipitated by CH_2Cl_2 /hexane mixture. 2-(4-Aminobutyl)-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-
35 yl)propyl]}carboxamido-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine was obtained as a yellowish powder (227 mg, 84%). M.p. 75-78 °C; Calcd for

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$C_{35}H_{46}N_6O_6 \cdot 1/2H_2O$: C 64.10, H 7.22, N 12.82; Found: C 63.99, H 6.82, N 12.67.

EXAMPLE 167

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2-(4-Aminobutyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (167). A solution of 7-azido-2-[(4-nitrophenyl)methylene]-3-oxoheptanoic acid 2-cyanoethyl ester (2.62 g, 7.06 mmol) and 3-aminocrotonamide (0.710 g, 7.06 mmol) in 50 EtOH was refluxed for 48 hrs. After the EtOH was removed in vacuo, the residue was dissolved in 100 ml of $CHCl_3$, washed with water (2x50 ml) and dried over Na_2SO_4 . After filtration and evaporation of solvent, 2-(4-azidobutyl)-5-carboxamido-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine was obtained as a brownish oil (2.42 g, 76% yield).

20 A solution of 2-(4-azidobutyl)-5-carboxamido-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine (2.42 g, 5.34 mmol) in 15 ml acetone was treated with 25 ml 1N aqueous KOH solution at 0 °C for 1 hr. The acetone was removed in vacuo, the aqueous layer was washed with $CHCl_3$ and acidified to pH=3 by 2N hydrochloric acid, the yellow precipitate was collected by filtration, washed with 10 ml of cold water and dried in vacuo to yield 1.40 g (65% yield) of 2-(4-azidobutyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid as a yellow powder.

A solution of 2-(4-azidobutyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (400 mg, 1.00 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (380 mg, 2.00 mmol) and 4-dimethylaminopyridine (130 mg, 1.00 mmol) in 20 ml of

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CH₂Cl₂ was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (300 mg, 1.02 mmol) in 5 ml of CH₂Cl₂ was added and the mixture was stirred at reflux overnight. The mixture was washed with water (20 ml), saturated aqueous NH₄Cl (3×20 ml), 20 ml 10% K₂CO₃ and 20 ml of brine. After drying over Na₂SO₄ and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO₂, MeOH: CHCl₃:1N NH₃ in MeOH, 6:90:3) and precipitated by CH₂Cl₂/hexanemixture. 2-(4-Azidobutyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (420 mg, 62%). M.p. 100 °C; Calcd. for C₃₈H₄₄N₈O₄: C 67.44, H 6.55, N 16.56; Found: C 67.14, H 6.33, N 16.30.

A solution of 2-(4-azidobutyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (90 mg, 0.133 mmol) in 5 ml of AcOEt was treated with 0.33 ml of 1M trimethylphosphine THF solution. The mixture was stirred at 0 °C for 1.5 hrs, 0.1 ml of water was then added and the mixture was stirred at room temperature for an additional 1.5 hrs. After most volatile materials were removed in vacuo, the residue was dissolved into AcOEt (50 ml), washed with 6N aqueous KOH (50 ml), brine (50 ml), and dried over K₂CO₃. After filtration and evaporation of solvent, product was precipitated by CH₂Cl₂/hexane mixture. 2-(4-Aminobutyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (82 mg, 95%). M.p. 95-99 °C; Calcd for C₃₈H₄₆N₈O₄·1/2H₂O: C 69.17, H 7.18, N 12.74; Found: C 69.12, H 6.86, N 12.43.

35

EXAMPLE 168

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2-(3-Aminopropyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (168). A solution of ethyl 4-bromobutyrate (10.0 g, 51.3 mmol), NaN₃ (6.66 g, 102 mmol) and 25 ml of water in 75 ml of MeOH was refluxed for 3.5 hrs. The MeOH was removed in vacuo and residue was partitioned between CHCl₃ (200 ml) and water (50 ml). The organic layer was separated and washed with water. After drying and evaporation of solvent, ethyl 4-azidobutyrate (7.94 g, 98.6%) was obtained as a colorless oil.

Ethyl 4-azidobutyrate (8.06 g, 51.3 mmol) and KOH (14.4 g, 0.256 mol) were dissolved into a mixture of 100 ml of water and 120 ml of MeOH. The solution was stirred at 0°C for 2 hrs and then MeOH was removed in vacuo. The aqueous layer was extracted by CHCl₃ (50 ml), acidified to pH=1 by 2N aqueous HCl and extracted by Et₂O (2×100 ml). The organic layers were combined, washed with water (100 ml) and dried over Na₂SO₄. After filtration and evaporation of solvent, 4-azidobutyric acid (5.30 g, 80%) was obtained as a colorless oil.

4-Azidobutyric acid (2.00 g, 15.5 mmol) in 15 ml of toluene was treated with oxalyl chloride (4.92 g, 38.7 mmol). The mixture was stirred at 50°C for 10 hrs. After removal of toluene in vacuo, crude 4-azidobutyric chloride was used for next reaction without further purifications.

30

To the solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (3.82 g, 26.5 mmol) and pyridine (4.20 g, 53.0 mmol) in 150 ml of CH₂Cl₂, was added dropwise a solution of crude 4-azidobutyric chloride (3.90 g, 26.5 mmol) in 30 ml of CH₂Cl₂ at 0 °C. The mixture was stirred at 0 °C for 1 hr then at room temperature for 1 hr. The solution was washed with 0.5N aqueous HCl (60 ml), water (60 ml)

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followed by brine (60 ml) and dried. After evaporation of solvent, 5-(4-azidobutanoyl)-2,2-dimethyl-1,3-dioxane-4,6-dione was obtained as a light pink oil (6.20 g, 92%).

5 5-(4-Azidobutanoyl)-2,2-dimethyl-1,3-dioxane-4,6-dione was heated with 3-hydroxypropionitrile (5.25 g, 72.0 mmol) at 80 °C until no more CO₂ was released. The reaction mixture was diluted with CH₂Cl₂ (100 ml), washed with water (100 ml) and brine (100 ml). After drying and
10 evaporation of solvent, the product was purified by chromatography (SiO₂, CHCl₃:MeOH=95:5), 4-azidobutanoylacetic acid 2-cyanoethyl ester was obtained as a yellowish oil (2.86 g, 53.2%).

15 A mixture of 4-azidobutanoylacetic acid 2-cyanoethyl ester (2.83 g, 12.6 mmol), 4-nitrobenzaldehyde (1.91 g, 12.6 mmol), piperidine (53 mg, 0.63 mmol) and acetic acid (38 mg, 0.63 mmol) was stirred at r.t. for 48 hrs. The product,
20 6-azido-2-[(4-nitrophenyl)methylene]-3-oxohexanoic acid 2-cyanoethyl ester was separated out as a brownish oil (2.16 g, 48%).

A solution of 6-azido-2-[(4-nitrophenyl)methylene]-3-oxohexanoic acid 2-cyanoethyl ester (2.16 g, 6.06 mmol)
25 and 3-aminocrotonamide (1.21 g, 12.1 mmol) in 50 EtOH was refluxed for 48 hrs. After the EtOH was removed in vacuo, the residue was dissolved in 150 ml of CHCl₃, washed with water (2x100 ml) and dried over Na₂SO₄. After filtration and evaporation of solvent, the product was
30 purified by chromatography (SiO₂, CHCl₃:MeOH=95:5). 2-(3-Azidopropyl)-5-carboxamido-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine was obtained as a yellow powder (1.28 g, 48% yield).

35 A solution of 2-(3-azidopropyl)-5-carboxamido-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine (1.28 g, 2.91 mmol) in 20 ml acetone

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was treated with 15 ml 1N aqueous KOH solution at 0 °C for 45 min. The acetone was removed in vacuo and the aqueous layer was acidified to pH=3 by 2N hydrochloric acid. The resulting yellow precipitate was collected by
5 filtration, washed with 10 ml of cold water and dried in vacuo to yield 800 mg (71% yield) of 2-(3-azidopropyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid as a yellow powder.

10

A solution of 2-(3-azidopropyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (300 mg, 0.78 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (297 mg, 1.55 mmol) and
15 4-dimethylaminopyridine (95 mg, 0.78 mmol) in 40 ml of CH₂Cl₂ was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (228 mg, 0.78 mmol) in 5 ml of CH₂Cl₂ was added and the mixture was stirred at reflux overnight. The mixture was
20 washed with water (30 ml), saturated aqueous NH₄Cl (3x30 ml), 10% K₂CO₃ (30 ml) and brine (30 ml). After drying over Na₂SO₄ and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO₂, MeOH: CHCl₃:1N NH₃ in MeOH, 6:90:3) and precipitated by
25 CH₂Cl₂/hexane mixture. 2-(3-Azidopropyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (300 mg, 58%). M.p. 99 °C (dec.); Calcd. for C₃₇H₄₂N₈O₄•3/4H₂O: C 65.71, H 6.48, N
30 16.57; Found: C 65.86, H 6.22, N 16.62.

A solution of 2-(3-azidopropyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (102
35 mg, 0.154 mmol) in 5 ml of AcOEt was treated with 0.4 ml of 1M trimethylphosphine THF solution. The mixture was stirred at 0 °C for 1.5 hrs, then 0.1 ml of water was

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added and the mixture was stirred at room temperature for an additional 1.5 hrs. After most volatile materials were removed in vacuo, the residue was dissolved into AcOEt (50 ml), washed with 6N aqueous KOH (50 ml) and
5 brine (50 ml), then dried over K_2CO_3 . After filtration and evaporation of solvent, the product was precipitated by CH_2Cl_2 /hexane mixture. 2-(3-Aminopropyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (88
10 mg, 90%). M.p. 97-100 °C; Calcd for $C_{37}H_{44}N_6O_4 \cdot 1/2H_2O$: C 68.82, H 7.02, N 13.01; Found: C 68.56, H 6.71, N 12.89.

EXAMPLE 169

15 2-(5-Aminopentyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (169). A solution of ethyl 6-bromohexanoate (10.0 g, 44.8 mmol), NaN_3 (5.83 g, 89.6
20 mmol) and 25 ml of water in 75 ml of MeOH was refluxed for 3.5 hrs. The MeOH was removed in vacuo and the residue was partitioned between $CHCl_3$ (200 ml) and water (50 ml). The organic layer was separated and washed with water. After drying (Na_2SO_4) and evaporation of solvent,
25 ethyl 6-azidohexanoate (8.59 g, 100%) was obtained as a colorless oil.

Ethyl 6-azidohexanoate (8.59 g, 44.8 mmol) and KOH (13.0 g, 0.231 mol) were dissolved into a mixture of 120 ml of
30 water and 180 ml of MeOH. The solution was stirred at 0 °C for 2 hrs then MeOH was removed in vacuo. The aqueous layer was extracted by $CHCl_3$ (2×100 ml), acidified to pH=1 by 2N aqueous HCl and extracted by Et_2O (2×100 ml). The organic layers were combined, washed with water
35 (100 ml) and dried over Na_2SO_4 . After filtration and evaporation of solvent, 6-azidohexanoic acid (6.56 g, 93%) was obtained as a colorless oil.

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6-Azidohexanoic acid (6.56 g, 41.7 mmol) in 15 ml of toluene was treated with oxalyl chloride (13.2 g, 104 mmol). The mixture was stirred at 50 °C for 10 hrs. After removal of toluene in vacuo, crude 6-azidohexanoic chloride was used for next reaction without further purification.

To a solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (6.31 g, 43.8 mmol) and 4-dimethylaminopyridine (5.60 g, 45.9 mmol) in 100 ml of CH_2Cl_2 was added dropwise a solution of crude 6-azidohexanoic chloride (7.32 g, 41.7 mmol) in 30 ml of CH_2Cl_2 at 0 °C. The mixture was stirred at 0 °C for 1 hr then at room temperature for 1 hr. The solution was washed with 0.5N aqueous HCl (100 ml), water (100 ml) followed by brine (100 ml) and dried over Na_2SO_4 . After filtration and evaporation of solvent, 5-(6-azidohexanoyl)-2,2-dimethyl-1,3-dioxane-4,6-dione was obtained as a light red oil (12.0 g, 100%).

5-(6-Azidohexanoyl)-2,2-dimethyl-1,3-dioxane-4,6-dione was heated with 3-hydroxypropionitrile (8.90 g, 125 mmol) at 80 °C until no more CO_2 was released. The reaction mixture was diluted with 150 ml of 2-propanol and 4-nitrobenzaldehyde (6.30 g, 41.7 mmol), piperidine (178 mg, 2.10 mmol) and acetic acid (125 mg, 2.10 mmol) were added. The mixture was stirred at room temperature for 48 hrs. After the solvent was evaporated, the residue was dissolved into CHCl_3 (200 ml), washed with water (150 ml) and brine (150 ml). After drying (Na_2SO_4) and evaporation of solvent, 8-azido-2-[(4-nitrophenyl)methylene]-3-oxooctanoic acid 2-cyanoethyl ester was obtained as a brownish oil (17.0 g, 100%).

A solution of 8-azido-2-[(4-nitrophenyl)methylene]-3-oxooctanoic acid 2-cyanoethyl ester (4.00 g, 10.4 mmol) and 3-aminocrotonamide (2.08 g, 20.8 mmol) in 100 ml EtOH was refluxed for 48 hrs. After the EtOH was removed in

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vacuo, the residue was dissolved in 150 ml of CHCl_3 , washed with water (2x100 ml) and dried over Na_2SO_4 . After filtration and evaporation of solvent, the product was purified by chromatography (SiO_2 , CHCl_3 : MeOH =95:5). 2-(5-Azidopentyl)-5-carboxamido-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine was obtained as a yellow oil (2.23 g, 47% yield).

A solution of 2-(5-azidopentyl)-5-carboxamido-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine (2.26 g, 5.44 mmol) in 10 ml acetone was treated with 25 ml 1N aqueous KOH solution at 0 °C for 1 hr. The acetone was removed in vacuo and the aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the resulting yellow precipitate was collected by filtration, washed with 10 ml of cold water and dried in vacuo to yield 1.50 g (67% yield) of 2-(5-azidopentyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid as a yellow powder.

A solution of 2-(5-azidopentyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (300 mg, 0.72 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (277 mg, 1.45 mmol) and 4-dimethylaminopyridine (88 mg, 0.72 mmol) in 40 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (213 mg, 0.72 mmol) in 5 ml of CH_2Cl_2 was added and the mixture was stirred at reflux overnight. The mixture was washed with water (30 ml), saturated aqueous NH_4Cl (3x30 ml), 10% K_2CO_3 (30 ml) and brine (30 ml). After drying over Na_2SO_4 and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , MeOH : CHCl_3 :1N NH_3 in MeOH , 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. 2-(5-Azidopentyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-

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diphenylpiperidin-1-yl)propyl}}carboxamidopyridine was obtained as a yellowish powder (300 mg, 58%). M.p. 85 °C (dec.); Calcd. for $C_{39}H_{46}N_8O_4 \cdot 3/4H_2O$: C 66.5, H 6.80, N 15.91; Found: C 66.45, H 6.63, N 16.03.

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A solution of 2-(5-azidopentyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl}}carboxamidopyridine (130 mg, 0.20 mmol) in 5 ml of AcOEt was treated with 0.60 ml of 1M trimethylphosphine THF solution. The mixture was stirred at 0 °C for 1.5 hrs then 0.10 ml of water was added and the mixture was stirred at room temperature for an additional 1.5 hrs. After most volatile materials were removed in vacuo, residue was dissolved into AcOEt (50 ml), washed with 6N aqueous KOH (50 ml) and brine (50 ml), then dried over K_2CO_3 . After filtration and evaporation of solvent, product was precipitated by CH_2Cl_2 /hexane mixture. 2-(5-Aminopentyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl}}carboxamidopyridine was obtained as a yellowish powder (110 mg, 85%). M.p. 75-78 °C; Calcd for $C_{39}H_{46}N_8O_4 \cdot 1/2H_2O$: C 69.52, H 7.33, N 12.47; Found: C 69.20, H 7.37, N 12.45.

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EXAMPLE 170

2-(4-Aminobutyl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl}}carboxamidopyridine (170). A solution of 7-azido-2-[(4-nitrophenyl)methylene]-3-oxoheptanoic acid 2-cyanoethyl ester (2.87 g, 7.73 mmol) and methyl 3-aminocrotonate (0.900 g, 7.73 mmol) in 50 ml of EtOH was refluxed for 48 hrs. After the EtOH was removed in vacuo, the residue was dissolved in 150 ml of $CHCl_3$, washed with water (2x100 ml) and dried over Na_2SO_4 . After filtration and evaporation of solvent, the product was purified by chromatography (SiO_2 , $CHCl_3$:MeOH=95:5). 2-(4-

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Azidobutyl)-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)pyridine was obtained as a yellow oil (2.43 g, 67% yield).

- 5 A solution of 2-(4-azidobutyl)-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)pyridine (1.38 g, 2.95 mmol) in 10 ml acetone was treated with 15 ml 1N KOH solution at 0°C for 1 hr. The acetone was removed in vacuo and the aqueous layer
10 was acidified to pH=3 by 2N hydrochloric acid, the resulting yellow precipitate was collected by filtration, washed with 10 ml of cold water and dried in vacuo to yield 750 mg (61% yield) of 2-(4-azidobutyl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)pyridine-3-
15 carboxylic acid as a yellow powder.

A solution of 2-(4-azidobutyl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (300 mg, 0.722 mmol), 1-(3-
20 dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (277 mg, 1.45 mmol) and 4-dimethylaminopyridine (132 mg, 1.08 mmol) in 40 ml of CH₂Cl₂ was stirred at r.t. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (213 mg, 0.72 mmol) in 5 ml of CH₂Cl₂ was
25 added and the mixture was stirred at reflux overnight. The mixture was washed with water (30 ml), saturated aqueous NH₄Cl (3×30 ml), 10% K₂CO₃ (30 ml) and brine (30 ml). After drying over Na₂SO₄ and evaporation of solvent, a yellowish oil was obtained which was purified by
30 chromatography (SiO₂, MeOH: CHCl₃:1N NH₃ in MeOH, 6:90:3) and precipitated by CH₂Cl₂/hexane mixture. 2-(4-Azidobutyl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a
35 yellowish powder (400 mg, 82%). M.p. 66-70 °C; Calcd. for C₃₉H₄₅N₇O₅·1/2H₂O: C 66.84, H 6.62, N 13.99; Found: C 66.80, H 6.48, N 13.89

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A solution of 2-(4-azidobutyl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (200 mg, 0.29 mmol) in 5 ml of AcOEt was treated with 0.87 ml of 1M trimethylphosphine THF solution. The mixture was stirred at 0 °C for 1.5 hrs then 0.05 ml of water was added and the mixture was stirred at room temperature for an additional 1.5 hrs. After most volatile materials were removed in vacuo, residue was dissolved in 50 ml of AcOEt, washed with 6N KOH (50 ml) and brine (50 ml), then dried over K₂CO₃. After filtration and evaporation of solvent, product was precipitated by CH₂Cl₂/hexane mixture. 2-(4-Aminobutyl)-1,4-dihydro-5-methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (150 mg, 78%). M.p. 89-93 °C; Calcd for C₃₉H₄₇N₅O₅·5/4H₂O: C 68.05, H 7.25, N 10.17; Found: C 68.14, H 7.08, N 10.11

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EXAMPLE 171

2-(4-Aminobutyl)-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (171). A solution of 2-(4-azidobutyl)-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)pyridine-3-carboxylic acid (300 mg, 0.72 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (276 mg, 1.44 mmol) and 4-dimethylaminopyridine (88 mg, 0.72 mmol) in 50 ml of CH₂Cl₂ was stirred at r.t. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (215 mg, 0.72 mmol) in 5 ml of CH₂Cl₂ was added and the mixture was stirred at reflux overnight. The mixture was washed with water (30 ml), saturated aqueous NH₄Cl (3×30 ml), 10% K₂CO₃ (30 ml) and brine (30 ml). After drying over Na₂SO₄ and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO₂, MeOH: CHCl₃:1N

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NH₃ in MeOH, 6:90:3) and precipitated by CH₂Cl₂/hexane mixture. 2-(4-Azidobutyl)-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a
5 yellowish powder (312 mg, 63%). M.p. 85-89 °C; Calcd. for C₃₉H₄₆N₈O₄: C 67.81, H 6.71, N 16.22; Found: C 67.42, H 6.45, N 15.89

A solution of 2-(4-azidobutyl)-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (310 mg, 0.45 mmol) in
10 5 ml of AcOEt was treated with 1.35 ml of 1M trimethylphosphine THF solution. The mixture was stirred at 0 °C for 1.5 hrs then 0.03 ml of water was added and
15 the mixture was stirred at room temperature for an additional 1.5 hrs. After most volatile materials were removed in vacuo, residue was dissolved into AcOEt (50 ml), washed with 6N KOH (50 ml) and brine (50 ml), then dried over K₂CO₃. After filtration and evaporation of
20 solvent, product was precipitated by CH₂Cl₂/hexane mixture. 2-(4-Aminobutyl)-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a
25 yellowish powder (267 mg, 89%). M.p. 85-89 °C; Calcd for C₃₉H₄₈N₆O₄: C 70.46, H 7.28, N 12.64; Found: C 70.25, H 7.62, N 12.34.

EXAMPLE 172

30 2-(4-Aminobutyl)-6-ethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (172). A solution of 6-ethyl-2,2-dimethyl-4H-1,3-dioxin-4-one (10.0 g, 64.0 mmol) in 20 ml of xylene was bubbled with
35 methylamine gas at 110 °C for 3 hrs. After cooling to room temperature, 5.3 ml of 1N HCl aqueous solution was added and the mixture was stirred at r.t. for 2 hrs. The

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organic layer was separated, the water layer was extracted by Et₂O (3×30 ml). The organic layers were combined and dried (Na₂SO₄). After evaporation of solvent, N-methyl propionylacetamide was obtained as a colorless oil (4.25 g, 51%).

A solution of N-methyl propionylacetamide (4.25 g, 32.9 mmol) in 30 ml xylene was bubbled with ammonia gas at 110 °C for 2 hrs. After cooling to room temperature, the mixture was diluted with 30 ml of CHCl₃ and dried (Na₂SO₄). After evaporation of solvent, N-methyl 3-amino-2-pentenamide was obtained as light-gray oil (4.15 g, 98%).

A solution of 7-azido-2-[(4-nitrophenyl)methylene]-3-oxoheptanoic acid 2-cyanoethyl ester (4.00 g, 10.8 mmol) and N-methyl 3-amino-2-pentenamide (1.52 g, 12.0 mmol) in 50 ml of EtOH was refluxed for 48 hrs. After the EtOH was removed in vacuo, the residue was dissolved in 150 ml of CHCl₃, washed with water (2×100 ml) and dried over Na₂SO₄. After filtration and evaporation of solvent, 2-(4-azidobutyl)-3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine was obtained as a brown oil (5.19 g, 99% yield).

A solution of 2-(4-azidobutyl)-3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (5.19 g, 10.8 mmol) in 20 ml acetone was treated with 30 ml 1N KOH solution at 0 °C for 1 hr. The acetone was removed in vacuo and the aqueous layer was washed with CHCl₃ (20 ml) and acidified to pH=3 by 2N hydrochloric acid, the resulting yellow precipitate was collected by filtration, washed with 10 ml of cold water and dried in vacuo to yield 3.21 g (69% yield) of 2-(4-azidobutyl)-6-ethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid as a yellow powder.

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A solution of 2-(4-azidobutyl)-6-ethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (500 mg, 1.17 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (450 mg, 2.34 mmol) and
5 4-dimethylaminopyridine (280 mg, 2.34 mmol) in 50 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (420 mg, 1.40 mmol) in 5 ml of CH_2Cl_2 was added and the mixture was stirred at reflux overnight. The mixture was
10 washed with water (30 ml), saturated aqueous NH_4Cl (3x30 ml), 10% K_2CO_3 (30 ml) and brine (30 ml). After drying over Na_2SO_4 and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by
15 CH_2Cl_2 /hexane mixture. 2-(4-Azidobutyl)-6-ethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (449 mg, 54%). M.p. 90-93 °C; Calcd. for $\text{C}_{40}\text{H}_{48}\text{N}_8\text{O}_4 \cdot 3/4\text{H}_2\text{O}$: C 66.88, H 6.94, N 15.66; Found: C 66.85, H 6.59, N 15.74.

A solution of 2-(4-azidobutyl)-6-ethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (402
25 mg, 0.57 mmol) in 5 ml of AcOEt was treated with 1.71 ml of 1M trimethylphosphine THF solution. The mixture was stirred at 0 °C for 1.5 hrs then 0.05 ml of water was added and the mixture was stirred at room temperature for
30 an additional 1.5 hrs. After most volatile materials were removed in vacuo, residue was dissolved into AcOEt (50 ml), washed with 6N KOH (50 ml) and brine (50 ml), then dried over K_2CO_3 . After filtration and evaporation of solvent, product was precipitated by CH_2Cl_2 /hexane
35 mixture. 2-(4-Aminobutyl)-6-ethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was

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obtained as a yellowish powder (350 mg, 90%). M.p. 105-109 °C; Calcd for $C_{40}H_{50}N_6O_4 \cdot 1/4H_2O$: C 70.30, H 7.45, N 12.30; Found: C 70.20, H 7.31, N 12.21.

5

EXAMPLE 173

6-Ethyl-1,4-dihydro-2-(4-methoxybutyl)-5-(N-methyl)carboxamido-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (173).

- 10 A solution of methyl 5-bromovalerate (10.0 g, 51.3 mmol), NaOMe (12.3 ml of 25% solution, 53.8 mmol) in 100 ml of MeOH was refluxed for 5 hrs. The MeOH was removed in vacuo and residue was partitioned between $CHCl_3$ (200 ml) and water (50 ml). The organic layer was separated and
15 washed with water (100 ml). After drying (Na_2SO_4) and evaporation of solvent, methyl 5-methoxyvalerate (7.33 g, 97.8%) was obtained as a colorless oil.

- Methyl 5-methoxyvalerate (7.33 g, 50.2 mmol) and KOH
20 (14.4 g, 0.256 mol) were dissolved into a mixture of 50 ml of water and 150 ml of MeOH. The solution was stirred at 0 °C for 2 hrs then MeOH was removed in vacuo. After washed by $CHCl_3$ (50 ml), the aqueous layer was acidified to pH=1 by 2N HCl and extracted by Et_2O (2×100 ml).
25 Organic layers were combined, washed with water (100 ml) and dried over Na_2SO_4 . After filtration and evaporation of solvent, 5-methoxyvaleric acid (5.27 g, 79.6%) was obtained as a colorless oil.

- 30 5-Methoxyvaleric acid (5.27 g, 39.9 mmol) in 15 ml of toluene was treated with oxalyl chloride (12.7 g, 99.8 mmol). The mixture was stirred at 50 °C for 10 hrs. After removal of toluene in vacuo, crude 5-methoxyvaleric chloride was used for next reaction without further
35 purification.

To a solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (5.77

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g, 40.0 mmol) and 4-dimethylaminopyridine (5.86 g, 44.0 mmol) in 100 ml of CH_2Cl_2 was added dropwise the solution of crude 5-methoxyvaleric chloride (6.00 g, 39.9 mmol) in 10 ml of CH_2Cl_2 at 0 °C. The mixture was stirred at 0 °C for 1 hr then at room temperature for an additional 1 hr. The solution was washed with 1N aqueous HCl (100 ml) and brine (250 ml). After dried over Na_2SO_4 and evaporation of solvent, 5-(5-methoxypentanoyl)-2,2-dimethyl-1,3-dioxane-4,6-dione was obtained as a light pink oil (9.20 g, 89%).

5-(5-Methoxypentanoyl)-2,2-dimethyl-1,3-dioxane-4,6-dione was heated with 3-hydroxypropionitrile (2.79 g, 39.2 mmol) at 80 °C until no more CO_2 was released. After cooling to room temperature, the mixture was diluted with 50 ml of 2-propanol and 4-nitrobenzaldehyde (5.40 g, 35.6 mmol), piperidine (150 mg, 1.78 mmol) and acetic acid (110 mg, 1.78 mmol) was added, the mixture was stirred at room temperature for 48 hrs. After evaporation of solvent, the product was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3=5:95$). 7-Methoxy-2-[(4-nitrophenyl)methylene]-3-oxoheptanoic acid 2-cyanoethyl ester was obtained as a pale-yellow oil (7.75 g, 60% yield).

A solution of 7-methoxy-2-[(4-nitrophenyl)methylene]-3-oxoheptanoic acid 2-cyanoethyl ester (3.87 g, 10.8 mmol) and N-methyl 3-amino-2-pentenamide (1.52 g, 11.9 mmol) in 40 ml of EtOH was refluxed for 48 hrs. After the EtOH was removed in vacuo, the residue was dissolved in 150 ml of CHCl_3 , washed with water (2x100 ml) and dried over Na_2SO_4 . After filtration and evaporation of solvent, the product was purified by chromatography (SiO_2 , $\text{CHCl}_3:\text{MeOH}=5:95$). 3-(2-Cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine was obtain as a yellow oil (3.60 g, 71% yield).

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A solution of 3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (3.60 g, 7.65 mmol) in 15 ml of acetone was treated with 20 ml of 1N aqueous KOH solution at 0°C for 1 hr. The acetone was removed in vacuo and the aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the resulting yellow precipitate was collected by filtration, washed with 10 ml of cold water and dried in vacuo to yield 1.99 g (63% yield) of 6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid as a yellow powder.

A solution of 6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (626 mg, 1.50 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (575 mg, 3.00 mmol) and 4-dimethylaminopyridine (367 mg, 3.00 mmol) in 60 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (530 mg, 1.80 mmol) in 10 ml of CH_2Cl_2 was added and the mixture was stirred at reflux overnight. The mixture was washed with water (30 ml), saturated NH_4Cl (3x30 ml), 30% K_2CO_3 (30 ml) and brine (30 ml). After dried over Na_2SO_4 and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. 6-Ethyl-1,4-dihydro-2-(4-methoxybutyl)-5-(N-methyl)carboxamido-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (530 mg, 51%). M.p. 98-102 °C; Calcd. for $\text{C}_{41}\text{H}_{51}\text{N}_5\text{O}_5\cdot\text{H}_2\text{O}$: C 69.17, H 7.50, N 9.84; Found: C 69.10, H 7.43, N 9.89.

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EXAMPLE 174

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6-Ethyl-1,4-dihydro-2-(4-methoxybutyl)-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (174). A solution of 6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (626 mg, 1.50 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (575 mg, 3.00 mmol) and 4-dimethylaminopyridine (367 mg, 3.00 mmol) in 60 ml of CH₂Cl₂ was stirred at room temperature. After 1 hr, a solution of 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (497 mg, 1.80 mmol) in 10 ml of CH₂Cl₂ was added and the mixture was stirred at reflux overnight. The mixture was washed with water (30 ml), saturated aqueous NH₄Cl (3×30 ml), 10% K₂CO₃ (30 ml) and brine (30 ml). After dried over Na₂SO₄ and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO₂, MeOH: CHCl₃:1N NH₃ in MeOH, 6:90:3) and precipitated by CH₂Cl₂/hexane mixture. The title compound was obtained as a yellowish powder (512 mg, 51%). M.p. 71-74 °C; Calcd. for C₃₇H₄₉N₅O₇: C 65.75, H 7.31, N 10.36; Found: C 65.47, H 7.37, N 10.22.

EXAMPLE 175

5-Carboxamido-6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (175). A solution of 7-methoxy-2-[(4-nitrophenyl)methylene]-3-oxoheptanoic acid 2-cyanoethyl ester (3.87 g, 10.8 mmol) and 3-amino-2-pentenamide (1.36 g, 11.9 mmol) in 40 ml of EtOH was refluxed for 48 hrs. After the EtOH was removed in vacuo, the residue was dissolved in 150 ml of CHCl₃, washed with water (2×100 ml) and dried over Na₂SO₄. After filtration and evaporation of solvent, 5-carboxamido-3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-4-(4-nitrophenyl)pyridine was obtained as

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a yellow oil (4.00 g, 81% yield).

A solution of 5-carboxamido-3-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-4-(4-nitrophenyl)pyridine (4.00 g, 8.76 mmol) in 15 ml of acetone was treated with 25 ml 1N aqueous KOH solution at 0°C for 1 hr. The acetone was removed in vacuo and the aqueous layer was washed with CHCl₃ (15 ml) then acidified to pH=3 by 2N hydrochloric acid, the resulting yellow precipitate was collected by filtration, washed with 10 ml of cold water and dried in vacuo to yield 1.69 g (48% yield) of 5-carboxamido-6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-4-(4-nitrophenyl)pyridine-3-carboxylic acid as a yellow powder.

15 A solution of 5-carboxamido-6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.50 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (192 mg, 1.00 mmol) and 20 4-dimethylaminopyridine (122 mg, 1.00 mmol) in 40 ml of CH₂Cl₂ was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (295 mg, 1.00 mmol) in 5 ml of CH₂Cl₂ was added and the mixture was stirred at reflux overnight. The mixture was 25 washed with water (20 ml), saturated aqueous NH₄Cl (3×20 ml), 10% K₂CO₃ (20 ml) and brine (20 ml). After dried over Na₂SO₄ and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO₂, MeOH: CHCl₃:1N NH₃ in MeOH, 6:90:3) and precipitated by 30 CH₂Cl₂/hexane mixture. 5-Carboxamido-6-ethyl-1,4-dihydro-2-(4-methoxybutyl)-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (188 mg, 50%). M.p. 80-84 °C; Calcd. for C₄₀H₄₉N₅O₅•1/2H₂O: C 69.94, H 7.32, N 10.17; 35 Found: C 69.56, H 7.03, N 10.19.

EXAMPLE 176

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5-Acetyl-2-(4-aminobutyl)-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (176). A solution of 7-azido-2-[(4-nitrophenyl)methylene]-3-oxoheptanoic acid 2-cyanoethyl ester (1.12 g, 3.00 mmol) and 4-amino-3-penten-2-one (330 mg, 3.30 mmol) in 20 ml of EtOH was refluxed for 48 hrs. After the EtOH was removed in vacuo, the residue was dissolved in 150 ml of CHCl₃, washed with water (2×100 ml) and dried over Na₂SO₄. After filtration and evaporation of solvent, the product was purified by chromatography (SiO₂, CHCl₃:MeOH= 5:95). 5-Acetyl-2-(4-azidobutyl)-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine was obtained as a yellow oil (1.05 g, 77% yield).

15 A solution of 5-acetyl-2-(4-azidobutyl)-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine (1.05 g, 2.32 mmol) in 10 ml of acetone was treated with 20 ml of 1N aqueous KOH solution at 0°C for 1 hr. The acetone was removed in vacuo and the aqueous layer was acidified to pH=3 by 2N hydrochloric acid, the resulting yellow precipitate was collected by filtration, washed with 10 ml of cold water and dried in vacuo to yield 0.60 g (60% yield) of 5-acetyl-2-(4-azidobutyl)-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid as a yellow powder.

30 A solution of 5-acetyl-2-(4-azidobutyl)-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.50 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (192 mg, 1.00 mmol) and 4-dimethylaminopyridine (122 mg, 1.00 mmol) in 40 ml of CH₂Cl₂ was stirred at room temperature. After 1 hr, a solution of 3-(4,4-diphenylpiperidin-1-yl)propylamine (162 mg, 0.55 mmol) in 5 ml of CH₂Cl₂ was added and the mixture was stirred at reflux overnight. The mixture was

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washed with water (20 ml), saturated aqueous NH_4Cl (3×20 ml), 10% K_2CO_3 (20 ml) and brine (20 ml). After dried over Na_2SO_4 and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 ,
5 MeOH: CHCl_3 :1N NH_3 in MeOH, 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture. 5-Acetyl-2-(4-azidobutyl)-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was obtained as a yellowish powder (126 mg, 37%).

10 A solution of 5-acetyl-2-(4-azidobutyl)-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine (126 mg, 0.19 mmol) in 5 ml of AcOEt was treated with 0.57 ml of 1M
15 trimethylphosphine THF solution. The mixture was stirred at 0 °C for 1.5 hrs then 0.02 ml of water was added and the mixture was stirred at room temperature for an additional 1.5 hrs. After most volatile materials were removed in vacuo, residue was dissolved into 50 ml of
20 AcOEt, washed with 6N aqueous KOH (50 ml) and brine (50 ml), then dried over K_2CO_3 . After filtration and evaporation of solvent, product was precipitated by CH_2Cl_2 /hexane mixture. 5-Acetyl-2-(4-aminobutyl)-1,4-dihydro-6-methyl-4-(4-nitrophenyl)-3-{N-[3-(4,4-diphenylpiperidin-1-yl)propyl]}carboxamidopyridine was
25 obtained as a yellowish powder (112 mg, 90%). M.p. 76-79 °C; Calcd for $\text{C}_{39}\text{H}_{47}\text{N}_5\text{O}_4 \cdot 3/4\text{H}_2\text{O}$: C 70.62, H 7.37, N 10.56; Found: C 70.56, H 6.96, N 10.40.

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EXAMPLE 177

2-(4-Aminobutyl)-5-carboxamido-1,4-dihydro-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-6-methyl-4-(4-nitrophenyl)pyridine
35 (177). A solution of 2-(4-azidobutyl)-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (416 mg, 1.04 mmol), 1-(3-dimethylaminopropyl)-3-

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ethylcarbodiimide hydrochloride (399 mg, 2.08 mmol) and 4-dimethylaminopyridine (177 mg, 1.04 mmol) in 50 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (254 mg, 1.04 mmol) in 5 ml of CH_2Cl_2 was added and the mixture was stirred at reflux overnight. The mixture was washed with water (20 ml), saturated aqueous NH_4Cl (3x20 ml), 10% K_2CO_3 (20 ml) and brine (20 ml). After dried over Na_2SO_4 and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ mixture. 2-(4-Azidobutyl)-5-carboxamido-1,4-dihydro-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-6-methyl-4-(4-nitrophenyl)pyridine was obtained as a yellowish powder (340 mg, 52%). M.p. 78-81 °C; Calcd. for $\text{C}_{34}\text{H}_{42}\text{N}_8\text{O}_6 \cdot 1/2\text{Et}_2\text{O}$: C 62.14, H 6.81, N 16.10; Found: C 62.42, H 6.33, N 15.85.

A solution of 2-(4-azidobutyl)-5-carboxamido-1,4-dihydro-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-6-methyl-4-(4-nitrophenyl)pyridine (150 mg, 0.23 mmol) in 5 ml of AcOEt was treated with 0.72 ml of 1M trimethylphosphine THF solution. The mixture was stirred at 0 °C for 1.5 hrs then 0.02 ml of water was added and the mixture was stirred at room temperature for an additional 1.5 hrs. After most volatile materials were removed in vacuo, residue was dissolved into 50 ml of AcOEt , washed with 6N KOH (50 ml) and brine (50 ml), then dried over K_2CO_3 . After filtration and evaporation of solvent, product was precipitated by CH_2Cl_2 /hexane mixture. 2-(4-Aminobutyl)-5-carboxamido-1,4-dihydro-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-6-methyl-4-(4-nitrophenyl)pyridine was obtained as a yellowish powder (110 mg, 76%). M.p. 81-84 °C; Calcd for $\text{C}_{34}\text{H}_{44}\text{N}_6\text{O}_6$: C 64.54, H 7.01, N 13.28; Found: C 64.29, H 6.87, N 13.22.

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EXAMPLE 178

5-Acetyl-2-(4-aminobutyl)-1,4-dihydro-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-6-methyl-4-(4-nitrophenyl)pyridine (178). A solution of 5-acetyl-2-(4-azidobutyl)-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (200 mg, 0.50 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (192 mg, 1.00 mmol) and 4-dimethylaminopyridine (122 mg, 1.00 mmol) in 40 ml of CH_2Cl_2 was stirred at room temperature. After 1 hr, a solution of 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (152 mg, 0.55 mmol) in 5 ml of CH_2Cl_2 was added and the mixture was stirred at reflux overnight. The mixture was washed with water (20 ml), saturated aqueous NH_4Cl (3x20 ml), 10% K_2CO_3 (20 ml) and brine (20 ml). After dried over Na_2SO_4 and evaporation of solvent, a yellowish oil was obtained, which was purified by chromatography (SiO_2 , $\text{MeOH}:\text{CHCl}_3:1\text{N NH}_3$ in MeOH , 6:90:3) and precipitated by CH_2Cl_2 /hexane mixture.

A solution of 5-acetyl-2-(4-azidobutyl)-1,4-dihydro-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-6-methyl-4-(4-nitrophenyl)pyridine (118 mg, 0.18 mmol) in 5 ml of AcOEt was treated with 0.54 ml of 1M trimethylphosphine THF solution. The mixture was stirred at 0 °C for 1.5 hrs then 0.02 ml of water was added and the mixture was stirred at room temperature for an additional 1.5 hrs. After most volatile materials were removed in vacuo, residue was dissolved into 50 ml of AcOEt , washed with 6N KOH (50 ml) and brine (50 ml), then dried over K_2CO_3 . After filtration and evaporation of solvent, product was precipitated by CH_2Cl_2 /hexane mixture. 5-Acetyl-2-(4-aminobutyl)-1,4-dihydro-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-6-methyl-4-(4-nitrophenyl)pyridine was obtained as a yellowish powder

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(98 mg, 86%). M.p. 62-65 °C; Calcd for $C_{35}H_{45}N_5O_6$: C 66.54, H 7.18, N 11.09; Found: C 66.34, H 7.40, N 10.87.

EXAMPLE 179

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4-Methoxycarbonyl-4-phenylpiperidine. To a stirred solution of H_2SO_4 (16 mL) in MeOH (400 mL), 4-phenyl-4-piperidinecarboxylic acid 4-methylbenzenesulfonate (37.7 g, 0.1 mole) was added and the mixture was stirred and
10 refluxed for 8 hours. Excess methanol was evaporated at reduced pressure and the residue was poured into a mixture of ice and 6N NaOH. The pH was adjusted to 10-11 by adding more 6N NaOH and extracted with CH_2Cl_2 (3 X 150 mL). The combined CH_2Cl_2 extracts were dried ($MgSO_4$) and
15 the solvent evaporated to leave the desired product as a viscous oil. The 1H -NMR showed it to be pure (20.2 g, 92%) and was used without any further purification.

3-(4-Methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine. A mixture of
20 4-methoxycarbonyl-4-phenylpiperidine (8.5 g, 0.039 mol), 3-bromopropylamine hydrobromide (12.7 g, 0.058 mol), potassium carbonate (13.475 g, 0.0957 mole), and KI (3.24 g, 0.0195 mol) in 1,4-dioxane (200 mL) was stirred and
25 refluxed for 24 hours. Dioxane was evaporated at reduced pressure, the residue was treated with ice-cold 6N NaOH (400 mL) and extracted with CH_2Cl_2 (4 X 120 mL). Solvent was evaporated from the combined dried (K_2CO_3) extracts and the residue was purified by column chromatography on
30 silica gel using $CHCl_3/MeOH/2M NH_3$ in MeOH (20:2:1) as the eluent to afford the product as a viscous oil (7.8 g, 72%).

2,6-Diethyl-1,4-dihydro-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (179). A mixture of

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2, 6 - diethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (0.15 g, 0.417 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.12 g, 0.626 mmol), 4-(N,N-dimethylamino)pyridine (0.056 g, 0.459 mmol), and 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (0.1268 g, 0.459 mmol) in CH_2Cl_2 (20 mL) was stirred and refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 150 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (90:8:5) as the eluent to afford the product as a yellow powder (0.118 g, 46%); mp 86-87 °C. Anal. Calcd for $\text{C}_{34}\text{H}_{43}\text{N}_5\text{O}_6 \cdot 0.8 \text{ H}_2\text{O}$: C, 64.60; H, 7.11; N, 11.08. Found: C, 64.63; H, 6.90; N, 10.98.

20.

EXAMPLE 180

2,6-Diethyl-1,4-dihydro-5-(N-ethyl)carboxamido-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (180). A mixture of 2,6-diethyl-1,4-dihydro-5-(N-ethyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (0.1557 g, 0.417 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.12 g, 0.626 mmol), 4-(N,N-dimethylamino)pyridine (0.056 g, 0.459 mmol), and 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (0.1268 g, 0.459 mmol) in CH_2Cl_2 (20 mL) was stirred and refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 150 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (90:8:5) as the

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eluent to afford the product as a yellow powder (0.115 g, 43.7%); mp 217 °C(d). Anal. Calcd for $C_{35}H_{45}N_5O_6 \cdot 0.1 CHCl_3$: C, 65.49; H, 7.06; N, 10.88. Found: C, 65.23; H, 6.81; N, 10.65.

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EXAMPLE 181

4-Ethoxycarbonyl-4-phenylpiperidine. To a stirred solution of H_2SO_4 (1.62 g, 16.56 mmol) in EtOH (200 mL),
 10 4-phenyl-4-piperidinecarboxylic acid 4-methylbenzenesulfonate (25 g, 66.23 mmol) was added and the mixture was stirred and refluxed for 12 h. Excess ethanol was evaporated at reduced pressure and the residue was poured into a mixture of ice and 6N NaOH.
 15 The pH was adjusted to 10-11 by adding more 6N NaOH and extracted with CH_2Cl_2 (3 X 100 mL). The combined CH_2Cl_2 extracts were dried ($MgSO_4$) and the solvent evaporated to leave the desired product as a colorless viscous oil, the 1H -NMR showed it to be pure (14.68 g, 95%) and was used
 20 without any further purification.

3-(4-Ethoxycarbonyl-4-phenylpiperidin-1-yl)propylamine. A mixture of 4-ethoxycarbonyl-4-phenylpiperidine (30.5 g, 0.131 mol), 3-bromopropylamine hydrobromide (42.93 g, 0.196 mol), potassium carbonate (36.14 g, 0.241 mole),
 25 and KI (10.8 g, 0.065 mol) in 1,4-dioxane (500 mL) was stirred and refluxed for 24 hours. Dioxane was evaporated at reduced pressure, the residue was treated with ice-cold 6N NaOH (400 mL) and extracted with CH_2Cl_2
 30 (4 X 120 mL). Solvent was evaporated from the combined dried (K_2CO_3) CH_2Cl_2 extracts and the residue was purified by column chromatography on silica gel using $CHCl_3/MeOH/2M NH_3$ in MeOH (20:2:1) as the eluent to afford the product as a viscous oil (24.2 g, 83.3%).

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**2,6-Diethyl-1,4-dihydro-3-{N-[3-(4-ethoxycarbonyl-4-phen-
 y l p i p e r i d i n e - 1 - y l) p r o p y l a m i n e] } p r o p y l a m i n e**

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eridin-1-yl)propyl]}carboxamido-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (181). A mixture of 2,6-diethyl-1,4-dihydro-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (0.15 g, 0.417 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.12 g, 0.626 mmol), 4-(N,N-dimethylamino)pyridine (0.056 g, 0.459 mmol), and 3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (0.1333 g, 0.459 mmol) in CH_2Cl_2 (20 mL) was stirred and refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 150 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (90:8:5) as the eluent to afford the product as a yellow powder (0.090 g, 34.2%); mp 95-97 °C. Anal. Calcd for $\text{C}_{35}\text{H}_{45}\text{N}_5\text{O}_6 \cdot 0.8 \text{ CH}_3\text{OH}$: C, 65.41; H, 7.39; N, 10.65. Found: C, 65.65; H, 7.11; N, 10.35.

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EXAMPLE 182

2,6-Diethyl-1,4-dihydro-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-5-(N-ethyl)carboxamido-4(4-nitrophenyl)pyridine (182). A mixture of 2,6-diethyl-1,4-dihydro-5-(N-ethyl)carboxamido-4-(4-nitrophenyl)pyridine-3-carboxylic acid (0.1557 g, 0.417 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.12 g, 0.626 mmol), 4-(N,N-dimethylamino)pyridine (0.056 g, 0.459 mmol), and 3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (0.1333 g, 0.459 mmol) in CH_2Cl_2 (20 mL) was stirred and refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 150 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash

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column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (90:8:5) as the eluent to afford the product as a yellow powder (0.115 g, 43%); mp 103-104 °C. Anal. Calcd for $\text{C}_{36}\text{H}_{47}\text{N}_5\text{O}_6 \cdot 1.0 \text{ H}_2\text{O}$: C, 65.14; H, 7.44; N, 10.55. Found: C, 65.02; H, 7.25; N, 10.42.

EXAMPLE 183

2-[(2-Azidoethoxy)methyl]-5-carboxamido-1,4-dihydro-3-{
 10 N - [3 -
 (4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carbox-
 amido-6-methyl-4-(4-nitrophenyl)pyridine (183). A
 mixture of 2-[(2-azidoethoxy)methyl]-
 5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitrophen-
 15 yl)pyridine-3-carboxylic acid (0.15 g, 0.373 mmol), DCC
 (0.1539 g, 0.746 mmol), 4-(N,N-dimethylamino)pyridine
 (0.050 g, 0.410 mmol), and
 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine
 (0.1237 g, 0.447 mmol) in CH_2Cl_2 (20 mL) was stirred and
 20 refluxed for 6 h. The mixture was cooled to room
 temperature, diluted to 150 mL with CH_2Cl_2 , washed with
 saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4).
 Solvent was evaporated from the CH_2Cl_2 solution and the
 product was purified by flash column chromatography on
 25 silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:3:1.5) as
 the eluent to afford the product as a yellow powder
 (0.208 g, 84.5%); mp 71-72 °C. Anal. Calcd for
 $\text{C}_{33}\text{H}_{40}\text{N}_8\text{O}_7 \cdot 1.2 \text{ H}_2\text{O}$: C, 58.09; H, 6.26; N, 16.42. Found: C,
 58.31; H, 6.25; N, 16.16.

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EXAMPLE 184

2-[(2-Azidoethoxy)methyl]-5-carboxamido-1,4-dihydro-3-{N-
 [3-(4-(4-methoxyphenyl)-4-phenylpiperidin-1-yl)prop-
 35 yl]}carboxamido-6-methyl-4-(4-nitrophenyl)pyridine (184).
 A mixture of 2-[(2-azidoethoxy)methyl]-5-carboxam-
 ido-1,4-dihydro-6-methyl-4-(4-nitrophenyl)pyridine-3-

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carboxylic acid (0.15 g, 0.373 mmol), DCC (0.1539 g, 0.746 mmol), 4-(N,N-dimethylamino)pyridine (0.050 g, 0.410 mmol), and 3-{4-(4-methoxyphenyl)-4-phenylpiperidin-1-yl}propylamine (0.1452 g, 0.448 mmol) in CH_2Cl_2 (20 mL) was stirred and refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 150 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:3:1.5) as the eluent to afford the product as a yellow powder (0.214 g, 81%); mp 105-107 °C. Anal. Calcd for $\text{C}_{38}\text{H}_{44}\text{N}_8\text{O}_6 \cdot 0.62 \text{ CHCl}_3$: C, 59.26; H, 5.74; N, 14.31. Found: C, 59.21; H, 5.93; N, 14.31.

EXAMPLE 185

2-[(2-Aminoethoxy)methyl]-5-carboxamido-1,4-dihydro-3-{
N [3 -
(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carbox-
amido-6-methyl-4-(4-nitrophenyl)pyridine (185). To a
stirred solution of 2-[(2-azidoethoxy)methyl]-5-carboxam-
ido-1,4-dihydro-3-{N-[3-
(4-methoxycarbonyl-4-phenylpiperidin-1-yl)prop-
yl]}carboxamido-6-methyl-4-(4-nitrophenyl)pyridine (0.165
g, 0.249 mmol) in EtOAc (5 mL) at 0 °C a solution of
trimethylphosphine in THF (1 M, 0.62 mL, 0.62 mmol) was
added and stirred for 10 minutes. Water (0.022 mL, 1.249
mmol) was added and the mixture was allowed to warm to
room temperature. After 3 hours, solvents were
evaporated and the residue was purified by column
chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in
MeOH (10:2:1) as the eluent to afford the product as a
yellow powder (0.075 g, 53%); mp 121-122 °C. Anal. Calcd
for $\text{C}_{33}\text{H}_{42}\text{N}_6\text{O}_7 \cdot 0.66 \text{ CHCl}_3 \cdot 0.66 \text{ H}_2\text{O}$: C, 55.73; H, 6.11; N,
11.59. Found: C, 55.44; H, 6.31; N, 11.88.

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EXAMPLE 186

2-[(2-Aminoethoxy)methyl]-5-carboxamido-1,4-dihydro-3-{
 N-[3-(4-(4-methoxyphenyl)-4-phenylpiperidin-1-yl)prop-
 5 yl]}carboxamido-6-methyl-4-(4-nitrophenyl)pyridine (186).
 To a stirred solution of
 2-[(2-azidoethoxy)methyl]-5-carboxamido-1,4-dihy-
 dro-3-{N-[3-(4-(4-methoxyphenyl)-4-phenylpiperid-
 in-1-yl)propyl]}carboxamido-6-methyl-4-(4-nitrophen-
 10 yl)pyridine (0.17 g, 0.239 mmol) in EtOAc (5 mL) at 0 °C
 a solution of trimethylphosphine in THF (1 M, 0.6 mL, 0.6
 mmol) was added and stirred for 10 minutes. Water (0.022
 mL, 1.249 mmol) was added and the mixture was allowed to
 warm to room temperature. After 3 hours, solvents were
 15 evaporated and the residue was purified by column
 chromatography on silica gel using CHCl₃/MeOH/2M NH₃ in
 MeOH (10:2:1) as the eluent to afford the product as a
 yellow powder (0.080 g, 49%); mp 141-142 °C. Anal. Calcd
 for C₃₈H₄₆N₆O₆·0.9 CHCl₃·0.9 NH₄Cl: C, 55.72; H, 6.07; N,
 20 11.52. Found: C, 55.68; H, 6.22; N, 11.31.

EXAMPLE 187

1,4-Dihydro-2,6-dimethyl-3-{N-[3-(4-methoxycarbon-
 25 y l - 4 - p h e n y l p i p e r
 idin-1-yl)propyl]}carboxamido-5-(N-methyl)carboxamido-4-
 -(4nitrophenyl)pyridine (187). A mixture of 1,4-di-
 hydro-2,6-dimethyl-5-(N-methyl)carboxamido-4-(4-nitro-
 phenyl)pyridine-3-carboxylic acid (0.4839 g, 1.46 mmol),
 30 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide
 hydrochloride (0.5598 g, 2.92 mmol), 4-(N,N-
 dimethylamino)pyridine (0.2675 g, 2.19 mmol), and
 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine
 (0.444 g, 1.607 mmol) in CH₂Cl₂ (40 mL) was stirred and
 35 refluxed for 6 hours. The mixture was cooled to room
 temperature, diluted to 150 mL with CH₂Cl₂, washed with
 saturated NH₄Cl solution (3 X 40 mL), and dried (MgSO₄).

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Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.605 mg, 70.3%); mp 122-123 °C. Anal. Calcd for $\text{C}_{32}\text{H}_{39}\text{N}_5\text{O}_6 \cdot 0.3 \text{ C}_4\text{H}_{10}\text{O} \cdot 0.9 \text{ H}_2\text{O}$: C, 63.48; H, 7.03; N, 11.15. Found: C, 63.76; H, 7.28; N, 11.31.

EXAMPLE 188

10 1, 4 - D i h y d r o - 2 , 6 - d i m e t h y l - 3 - { N - [3 -
(4 - e t h o x y c a r b o n y l - 4 - p h e n y l -
p i p e r i d i n - 1 - y l) p r o p y l] } c a r b o x a m i d o - 5 - (N - m e t h y l) c a r b o x a m i d o - 4 - (4 n i t r o p h e n y l) p y r i d i n e (1 8 8) . A m i x t u r e o f
15 1 , 4 - d i h y d r o - 2 , 6 - d i m e t h y l - 5 - (N - m e t h y l) c a r b o x a m i d o - 4 - (4 - n i t r o p h e n y l) p y r i d i n e - 3 - c a r b o x y l i c
a c i d (0 . 4 5 0 g , 1 . 3 6 m m o l) , 1 - (3 - d i m e t h y l a m i n o p r o p y l) - 3 -
e t h y l c a r b o d i i m i d e h y d r o c h l o r i d e (0 . 5 2 0 7 g , 2 . 7 2 m m o l) , 4 -
(N , N - d i m e t h y l a m i n o) p y r i d i n e (0 . 2 8 5 9 g , 2 . 3 4 m m o l) , a n d
20 3 - (4 - e t h o x y c a r b o n y l - 4 - p h e n y l p i p e r i d i n - 1 - y l) p r o p y l a m i n e
(0 . 4 7 3 g , 1 . 6 3 m m o l) i n CH_2Cl_2 (4 0 m L) w a s s t i r r e d a n d
r e f l u x e d f o r 6 h o u r s . T h e m i x t u r e w a s c o o l e d t o r o o m
t e m p e r a t u r e , d i l u t e d t o 2 1 0 m L w i t h CH_2Cl_2 , w a s h e d w i t h
s a t u r a t e d NH_4Cl s o l u t i o n (3 X 3 0 m L) , a n d d r i e d (MgSO_4) .
25 S o l v e n t w a s e v a p o r a t e d f r o m t h e CH_2Cl_2 s o l u t i o n a n d t h e
p r o d u c t w a s p u r i f i e d b y f l a s h c o l u m n c h r o m a t o g r a p h y o n
s i l i c a g e l u s i n g $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ i n M e O H (1 0 0 : 3 . 5 : 1 . 7 5)
a s t h e e l u e n t t o a f f o r d t h e p r o d u c t a s a y e l l o w p o w d e r
(0 . 6 0 0 g , 7 3 %) ; m p 1 1 2 - 1 1 3 ° C . A n a l . C a l c d f o r
30 $\text{C}_{33}\text{H}_{41}\text{N}_5\text{O}_6 \cdot 0.075 \text{ C}_6\text{H}_{12} \cdot 0.75 \text{ H}_2\text{O}$: C, 64.43; H, 7.02; N, 11.23.
F o u n d : C , 6 4 . 2 9 ; H , 7 . 0 4 ; N , 1 0 . 9 5 .

EXAMPLE 189

35 2 - [(2 - A z i d o e t h o x y) m e t h y l] - 5 - (2 -
c y a n o e t h o x y c a r b o n y l) - 3 - { N - [3 -
(4 - e t h o x y c a r b o n y l - 4 - p h e n y l p i p e r i d i n - 1 - y l) p r o p y l] } c a r b o x

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amido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine. A mixture of 2-[(2-azidoethoxy)methyl]-5-(2-cyanoethoxycarbonyl)-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (1.06 g, 2.25 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.864 g, 4.507 mmol), 4-(N,N-dimethylamino)pyridine (0.550 g, 4.507 mmol), and 3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (0.784 g, 2.7 mmol) in CH_2Cl_2 (20 mL) was stirred and refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 150 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M}$ NH_3 in MeOH (100:3:1.5) as the eluent to afford the product as a yellow powder (1.24 g, 74%). The $^1\text{H-NMR}$ showed this product to be pure and was used in the subsequent step without any further purification.

20 2-[(2-Azidoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine-5-carboxylic Acid (189).
a well-stirred solution of
25 2-[(2-azidoethoxy)methyl]-5-(2-cyanoethoxycarbonyl)-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine (1.29 g, 1.74 mmol) in dioxane (25 mL) at 0 °C, aqueous 1N NaOH (5.21 mL, 5.21 mmol) was added and the stirring was continued. After 30 min, solvent was evaporated at reduced pressure at 0 °C and to the residue 1N HCl was added to adjust the pH to 6-7. The yellow precipitate formed was filtered and dried under vacuum. The filtrate
35 was extracted with CH_2Cl_2 (10 mL), dried (MgSO_4) and the solvent evaporated. The combined yield was 1.18 g (96.7%); mp 109-110 °C. Anal. Calcd for $\text{C}_{35}\text{H}_{43}\text{N}_7\text{O}_8 \cdot 0.4$

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$C_4H_8O_2 \cdot 0.6 NaCl$: C, 57.82; H, 6.13; N, 12.90. Found: C, 57.66; H, 6.19; N, 12.70.

EXAMPLE 190

5
2-[(2-Azidoethoxy)methyl]-5-carboxamido-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine (190). A mixture of 2-[(2-azidoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine-5-carboxylic acid (0.10 g, 0.145 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.056 g, 0.29 mmol), 4-(N,N-dimethylamino)pyridine (0.0354 g, 0.29 mmol), and 40% aqueous NH_3 (0.064 g, 0.725 mmol) in CH_2Cl_2 (20 mL) was stirred overnight. The reaction mixture was diluted to 170 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried ($MgSO_4$). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $CHCl_3/MeOH/2M NH_3$ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.083 g, 83%); mp 63-64 °C. Anal. Calcd for $C_{35}H_{44}N_8O_7 \cdot 0.3 C_6H_{12}O_5 \cdot 0.5 H_2O$: C, 60.53; H, 6.82; N, 15.34. Found: C, 60.69; H, 6.65; N, 15.08.

EXAMPLE 191

2-[(2-Azidoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (191). A mixture of 2-[(2-azidoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine-5-carboxylic acid (0.10 g, 0.145 mmol), 1-(3-dimethylaminopropyl)-3-

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ethylcarbodiimide hydrochloride (0.056 g, 0.29 mmol), 4-(N,N-dimethylamino)pyridine (0.0354 g, 0.29 mmol), and aqueous 40% methylamine (0.0563 g, 0.725 mmol) in CH_2Cl_2 (20 mL) was stirred overnight. The reaction mixture was
 5 diluted to 170 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:4:2) as the eluent to
 10 afford the product as a yellow powder (0.086 g, 84.4%); mp 67-68 °C. Anal. Calcd for $\text{C}_{36}\text{H}_{46}\text{N}_8\text{O}_7 \cdot 0.4 \text{H}_2\text{O}$: C, 60.90; H, 6.64; N, 15.78. Found: C, 60.95; H, 6.42; N, 15.42.

EXAMPLE 192

15 2-[(2-Aminoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenyl-piperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-5-(N-ethyl)carboxamido-4-(4-nitrophenyl)pyridine (192). A
 20 mixture of 2-[(2-azidoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenyl-piperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine-5-carboxylic acid (0.10 g, 0.145 mmol), 1-(3-dimethylaminopropyl)-3-
 25 ethylcarbodiimide hydrochloride (0.056 g, 0.29 mmol), 4-(N,N-dimethylamino)pyridine (0.0354 g, 0.29 mmol), and aqueous 70% methylamine (0.0373 g, 0.58 mmol) in CH_2Cl_2 (20 mL) was stirred overnight. The reaction mixture was diluted to 170 mL with CH_2Cl_2 , washed with saturated NH_4Cl
 30 solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution, the residue was redissolved in EtOAc (5 mL) and cooled to 0 °C. To this, a solution of trimethylphosphine in THF (1 M, 0.32 mL, 0.32 mmol) was added and stirred for 10 minutes. Water
 35 (0.0095 mL, 0.53 mmol) was added and the mixture was allowed to warm to room temperature. After 3 hours, solvents were evaporated and the residue was purified by

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column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (18:2:1) as the eluent to afford the product as a yellow powder (0.091 g, 91%); mp 112-114 °C. Anal. Calcd for $\text{C}_{37}\text{H}_{50}\text{N}_6\text{O}_8 \cdot 0.18 \text{ C}_6\text{H}_{14} \cdot 1.8 \text{ H}_2\text{O}$: C, 61.94; H, 7.61; N, 13.38. Found: C, 61.97; H, 7.59; N, 11.19.

EXAMPLE 193

2-[(2-Aminoethoxy)methyl]-5-carboxamido-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine (193). To a stirred solution of 6-ethyl-1,4-dihydro-2-[(2-azidoethoxy)methyl]-5-carboxamido-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (0.073 g, 0.106 mmol) in EtOAc (5 mL) at 0 °C a solution of trimethylphosphine in THF (1 M, 0.32 mL, 0.32 mmol) was added and stirred for 10 minutes. Water (0.0095 mL, 0.53 mmol) was added and the mixture was allowed to warm to room temperature. After 3 hours, solvents were evaporated and the residue was purified by column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (25:4:2) as the eluent to afford the product as a yellow powder (0.027 g, 38.4%); mp 87-89 °C. Anal. Calcd for $\text{C}_{35}\text{H}_{46}\text{N}_6\text{O}_7 \cdot 0.4 \text{ CHCl}_3$: C, 59.84; H, 6.58; N, 11.83. Found: C, 59.74; H, 6.85; N, 11.56.

EXAMPLE 194

2-[(2-Aminoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (194). To a stirred solution of 2-[(2-azidoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-

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ro-6-ethyl-5-(N-methyl)carboxamido-4-(4-nitrophenyl)pyridine (0.076 g, 0.108 mmol) in EtOAc (5 mL) at 0 °C a solution of trimethylphosphine in THF (1 M, 0.32 mL, 0.32 mmol) was added and stirred for 10 minutes. Water (0.0095 mL, 0.53 mmol) was added and the mixture was allowed to warm to room temperature. After 3 hours, solvents were evaporated and the residue was purified by column chromatography on silica gel using CHCl₃/MeOH/2M NH₃ in MeOH (25:4:2) as the eluent to afford the product as a yellow powder (0.018 g, 24.6%); mp 51-53 °C. Anal. Calcd for C₃₆H₄₈N₆O₇·0.12 C₆H₁₂·1.2 H₂O: C, 62.25; H, 7.37; N, 11.86. Found: C, 62.02; H, 7.12; N, 11.58.

EXAMPLE 195

2-[(2-Azidoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-5-methoxycarbonyl-4-(4-nitrophenyl)pyridine (195). A mixture of 2-[(2-azidoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine-5-carboxylic acid (0.10 g, 0.145 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.056 g, 0.29 mmol), 4-(N,N-dimethylamino)pyridine (0.0354 g, 0.29 mmol), and methanol (0.046 g, 1.45 mmol) in CH₂Cl₂ (10 mL) was stirred and refluxed for 12 hours. The reaction mixture was diluted to 160 mL with CH₂Cl₂, washed with saturated NH₄Cl solution (3 X 40 mL), and dried (MgSO₄). Solvent was evaporated from the CH₂Cl₂ solution and the product was purified by flash column chromatography on silica gel using CHCl₃/MeOH/2M NH₃ in MeOH (100:2:1) as the eluent to afford the product as a yellow powder (0.082 g, 80.4%); mp 56-57 °C. Anal. Calcd for C₃₆H₄₅N₇O₈·0.54 CHCl₃: C, 57.13; H, 5.97; N, 12.76. Found: C, 57.39; H, 6.14; N, 12.41.

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EXAMPLE 196

2-[(2-Aminoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine-5-carboxylic Acid (196). To a stirred solution of 2-[(2-azidoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-4-(4-nitrophenyl)pyridine-5-carboxylic acid (0.050 g, 0.0725 mmol) in EtOAc (5 mL) at 0 °C a solution of trimethylphosphine in THF (1 M, 0.217 mL, 0.217 mmol) was added and stirred for 10 minutes. Water (0.0095 mL, 0.53 mmol) was added and the mixture was allowed to warm to room temperature. After 3 h, solvents were evaporated and the residue was purified by column chromatography on silica gel using CHCl₃/MeOH/2M NH₃ in MeOH (25:4:2) as the eluent to afford the product as a yellow powder (0.018 g, 37.4%); mp 103-105 °C. Anal. Calcd for C₃₅H₄₅N₅O₈.0.35 CHCl₃: C, 60.18; H, 6.48; N, 9.93. Found: C, 60.08; H, 6.42; N, 10.07.

EXAMPLE 197

2-[(2-Aminoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-5-methoxycarbonyl-4-(4-nitrophenyl)pyridine (197). To a stirred solution of 2-[(2-azidoethoxy)methyl]-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-6-ethyl-5-methoxycarbonyl-4-(4-nitrophenyl)pyridine (0.092 g, 0.13 mmol) in EtOAc (5 mL) at 0 °C a solution of trimethylphosphine in THF (1 M, 0.65 mL, 0.65 mmol) was added and stirred for 10 minutes. Water (0.047 mL, 2.6 mmol) was added and the mixture was allowed to warm to room temperature. After 3 hours, solvents were evaporated and the residue was

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purified by column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (25:4:2) as the eluent to afford the product as a yellow powder (0.020 g, 22.7%); mp 45-47 °C. Anal. Calcd for $\text{C}_{36}\text{H}_{47}\text{N}_5\text{O}_8 \cdot 0.8 \text{ H}_2\text{O}$: C, 62.47; H, 7.08; N, 10.12. Found: C, 62.58; H, 7.01; N, 9.86.

EXAMPLE 198

5-Carboxamido-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (198). A mixture of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (0.60 g, 1.89 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.725 g, 3.78 mmol), 4-(N,N-dimethylamino)pyridine (0.462 g, 3.78 mmol), and 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (0.679 g, 2.457 mmol) in CH_2Cl_2 (40 mL) was stirred and refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 190 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.730 g, 67%); mp 120-121 °C. Anal. Calcd for $\text{C}_{31}\text{H}_{37}\text{N}_5\text{O}_6 \cdot 0.7 \text{ C}_6\text{H}_{12} \cdot 1.05 \text{ H}_2\text{O}$: C, 64.70; H, 7.33; N, 10.72. Found: C, 64.71; H, 7.25; N, 10.50.

EXAMPLE 199

5-Carboxamido-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (199). A mixture of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (0.60 g, 1.89 mmol), 1-(3-

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dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.725 g, 3.78 mmol), 4-(N,N-dimethylamino)pyridine (0.462 g, 3.78 mmol), and 3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (0.714 g, 2.46 mmol) in CH_2Cl_2 (40 mL) was stirred and refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 190 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.660 g, 59.3%); mp 118-120 °C. Anal. Calcd for $\text{C}_{32}\text{H}_{32}\text{N}_5\text{O}_6 \cdot 0.5 \text{ C}_6\text{H}_{12} \cdot 0.5 \text{ H}_2\text{O}$: C, 65.61; H, 7.24; N, 10.93. Found: C, 65.67; H, 7.25; N, 10.69.

EXAMPLE 200

5-Carboxamido-1,4-dihydro-2,6-diethyl-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (200). A mixture of 5-carboxamido-1,4-dihydro-2,6-diethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (0.80 g, 2.415 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.926 g, 4.289 mmol), 4-(N,N-dimethylamino)pyridine (0.524 g, 4.289 mmol), and 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (0.80 g, 2.898 mmol) in CH_2Cl_2 (40 mL) was stirred and refluxed for 6 h. The mixture was cooled to room temperature, diluted to 190 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.950 g, 70%); mp 112-114 °C. Anal. Calcd for $\text{C}_{33}\text{H}_{41}\text{N}_5\text{O}_6 \cdot 0.37 \text{ C}_6\text{H}_{10}\text{O} \cdot 0.41 \text{ H}_2\text{O}$: C, 64.86; H, 7.18; N, 10.97.

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Found: C, 65.13; H, 7.09; N, 10.68.

EXAMPLE 201

5 5-Acetyl-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-methoxy-
carbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-
(4-nitrophenyl)pyridine (201). A mixture of
5 - a c e t y l - 1 , 4 - d i h y d r o - 2 , 6 -
dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid
10 (0.70 g, 2.21 mmol), 1-(3-dimethylaminopropyl)-3-
ethylcarbodiimide hydrochloride (0.849 g, 4.43 mmol), 4-
(N,N-dimethylamino)pyridine (0.541 g, 4.43 mmol), and
3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine
(0.732 g, 2.65 mmol) in CH_2Cl_2 (40 mL) was stirred and
15 refluxed for 6 hours. The mixture was cooled to room
temperature, diluted to 190 mL with CH_2Cl_2 , washed with
saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4).
Solvent was evaporated from the CH_2Cl_2 solution and the
product was purified by flash column chromatography on
20 silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:4:2) as
the eluent to afford the product as a yellow powder
(0.880 g, 70%); mp 94-95 °C. Anal. Calcd for $\text{C}_{32}\text{H}_{38}\text{N}_4\text{O}_6 \cdot 0.4$
 H_2O : C, 66.11; H, 6.72; N, 9.63. Found: C, 65.93; H,
6.55; N, 9.53.

25

EXAMPLE 202

5-Acetyl-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-ethoxycar-
bonyl-4-phenylpiperidin-1-yl)propyl]}carbox-
30 amido-4-(4-nitrophenyl)pyridine (202). A mixture of
5 - a c e t y l - 1 , 4 - d i h y d r o - 2 , 6 - d i m e t h y l -
4-(4-nitrophenyl)pyridine-3-carboxylic acid (0.70 g,
2.21 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide
hydrochloride (0.849 g, 4.43 mmol), 4-(N,N-
35 dimethylamino)pyridine (0.541 g, 4.43 mmol), and
3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propylamine
(0.770 g, 2.65 mmol) in CH_2Cl_2 (40 mL) was stirred and

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refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 190 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.890 g, 68.4%); mp 87-88 °C. Anal. Calcd for $\text{C}_{33}\text{H}_{40}\text{N}_4\text{O}_6 \cdot 0.6 \text{ H}_2\text{O}$: C, 66.11; H, 6.93; N, 9.35. Found: C, 65.95; H, 6.84; N, 9.22.

202 (-) and 202 (+):

(-)-5-Acetyl-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine and (+)-5-Acetyl-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine. Racemic 5-acetyl-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine was separated on a chiral HPLC column Chiralpak AS (20 X 250 mm) as follows: The column was pre-equilibrated with 10% EtOH in hexane at 40 °C with an isocratic elution of 9 mL/minutes. The racemate (ca 20 mg) was dissolved in 1:2 ethanol/hexane (10 mL) and injected. Ten injections were made to obtain about 100 mg of each enantiomers. The first enantiomer to elute was the (-)-enantiomer (retention time, about 43 to 49 min) and the second major peak accounted for the (+)-enantiomer (retention time, about 57-67 min). Solvents were evaporated and the products were dried under vacuum. (-)-enantiomer: $[\alpha]_D = -151.24$ (MeOH, 1.45 g/100 mL); mp 89-90 °C. Anal. Calcd for $\text{C}_{33}\text{H}_{40}\text{N}_4\text{O}_6$: C, 67.33; H, 6.85; N, 9.52. Found: C, 67.12; H, 6.87; N, 9.33. (+)-enantiomer: $[\alpha]_D = +146.5$ (MeOH, 1.40 g/100 mL); mp

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89-90 °C. Anal. Calcd for $C_{33}H_{40}N_4O_6$: C, 67.33; H, 6.85; N, 9.52. Found: C, 67.09; H, 6.68; N, 9.33.

EXAMPLE 203

5 5-(2-Cyanoethoxycarbonyl)-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (203). A mixture of
 10 5-(2-cyanoethoxycarbonyl)-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (1.568 g, 4.22 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.62 g, 8.44 mmol), 4-(N,N-dimethylamino)pyridine (1.03 g, 8.44 mmol), and
 15 3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propylamine (1.40 g, 5.066 mmol) in CH_2Cl_2 (100 mL) was stirred and refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 200 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried ($MgSO_4$).
 20 Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $CHCl_3/MeOH/2M NH_3$ in MeOH (1.76 g, 66%); mp 73-74 °C. Anal. Calcd for $C_{34}H_{39}N_5O_7 \cdot 0.25 CH_2Cl_2 \cdot 1.25 H_2O$: C, 61.59; H, 6.26; N, 10.43. Found: C, 61.23; H,
 25 6.05; N, 10.21.

EXAMPLE 204

1,4-Dihydro-2,6-dimethyl-3-{N-[3-(4-methoxy-
 30 carbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine-5-carboxylic acid (204). To a well-stirred solution of 5-(2-cyanoethoxycarbonyl)-1,4-dihydro-2,6-dimethyl-3-{N-[3-(
 (4 - m e t h o x y -
 35 carbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (1.70 g, 2.70 mmol) in dioxane (15 mL) at 0 °C, aqueous 1N NaOH (5.4 mL) was added and the

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stirring was continued. After 30 min, most of the solvent was evaporated under reduced pressure and residue was treated with ice-cold 1N HCl to adjust the pH to 6-7. The yellow precipitate formed was filtered and dried under vacuum (1.35 g, 86%); mp 139-141 °C. Anal. Calcd for $C_{31}H_{37}N_4O_7 \cdot 0.4 CHCl_3 \cdot 1.6 H_2O$: C, 57.74; H, 6.11; N, 8.58. Found: C, 57.98; H, 6.31; N, 10.41.

EXAMPLE 205

10 1,4-Dihydro-2,6-dimethyl-5-(N-ethyl)carboxamido-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (205). A mixture of
15 1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine-5-carboxylic acid (0.70 g, 1.222 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.469 g, 2.445 mmol), 4-(N,N-dimethylamino)pyridine (0.299 g, 2.445 mmol), and
20 70% aqueous ethylamine (0.275 g, 4.277 mmol) in CH_2Cl_2 (40 mL) was stirred at room temperature for 14 hours, diluted to 150 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried ($MgSO_4$). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by
25 flash column chromatography on silica gel using $CHCl_3/MeOH/2M NH_3$ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.36 g, 41.5%); mp 117-118 °C. Anal. Calcd for $C_{33}H_{41}N_5O_6 \cdot 0.25 C_6H_{12} \cdot 0.05 CH_2Cl_2 \cdot 0.25 H_2O$: C, 65.51; H, 7.10; N, 11.05. Found: C,
30 65.66; H, 7.34; N, 10.75.

EXAMPLE 206

1,4-Dihydro-2,6-dimethyl-5-methoxycarbonyl-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (206). A mixture of 1,4-dihydro-2,6-dimethyl-3-{N[3-

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(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl}}carboxamido-4-(4-nitrophenyl)pyridine-5-carboxylic acid (0.10 g, 0.174 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.0666 g, 0.347 mmol),
5 4-(N,N-dimethylamino)pyridine (0.0424 g, 0.347 mmol), and methanol (1 mL) in CH₂Cl₂ (40 mL) was stirred and refluxed for 14 hours and cooled. The reaction mixture was diluted to 150 mL with CH₂Cl₂, washed with saturated NH₄Cl solution (3 X 40 mL), and dried (MgSO₄). Solvent was
10 evaporated from the CH₂Cl₂ solution and the product was purified by flash column chromatography on silica gel using CHCl₃/MeOH/2M NH₃ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.045 g, 44%); mp 83-84 °C. Anal. Calcd for C₃₃H₃₈N₄O₇·0.2 C₆H₁₂·0.4 H₂O: C,
15 64.87; H, 6.76; N, 9.11. Found: C, 65.01; H, 6.68; N, 8.82.

EXAMPLE 207

20 1,4-Dihydro-2,6-dimethyl-5-(2-hydroxyethoxycarbonyl)-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl}}carboxamido-4-(4-nitrophenyl)pyridine (207). A mixture of 1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl}}carboxamido-4-(4-nitrophenyl)pyridine-5-carboxylic acid (0.10 g, 0.174 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.0666 g, 0.347 mmol), 4-(N,N-dimethylamino)pyridine (0.0424 g, 0.347 mmol), and ethylene glycol (1 mL) in
25 CH₂Cl₂ (40 mL) was stirred and refluxed for 14 hours and cooled. The reaction mixture was diluted to 150 mL with CH₂Cl₂, washed with saturated NH₄Cl solution (3 X 40 mL), and dried (MgSO₄). Solvent was evaporated from the CH₂Cl₂ solution and the product was purified by flash column
30 chromatography on silica gel using CHCl₃/MeOH/2M NH₃ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.052 g, 48%); mp 90-91 °C. Anal. Calcd

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for $C_{33}H_{40}N_4O_8 \cdot 0.8 H_2O$: C, 62.41; H, 6.60; N, 8.82. Found: C, 62.65; H, 6.86; N, 8.54.

EXAMPLE 208

5 1,4-Dihydro-2,6-dimethyl-5-ethoxycarbonyl-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (208). A mixture of
 10 1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine-5-carboxylic acid (0.10 g, 0.174 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.0666 g, 0.347 mmol),
 15 4-(N,N-dimethylamino)pyridine (0.0424 g, 0.347 mmol), and ethanol (1 mL) in CH_2Cl_2 (40 mL) was stirred and refluxed for 14 hours and cooled. The reaction mixture was diluted to 150 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 40 mL), and dried ($MgSO_4$). Solvent was
 20 evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $CHCl_3/MeOH/2M NH_3$ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.055 g, 53%); mp 73-75 °C. Anal. Calcd for $C_{33}H_{40}N_4O_7 \cdot 0.25 C_6H_{12} \cdot 0.5 H_2O$: C,
 25 65.28; H, 6.99; N, 8.83. Found: C, 65.40; H, 7.03; N, 8.66.

EXAMPLE 209

30 5-Carboxamido-3-{N-[3-(4-(2-cyanoethoxycarbonyl)-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine (209). A mixture of
 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (0.415 g, 1.31 mmol),
 35 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.502 g, 2.62 mmol), 4-(N,N-

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dimethylamino)pyridine (0.640 g, 5.24 mmol), and 3-{4-(2-cyanoethoxycarbonyl)-4-phenylpiperidin-1-yl}propylamine.HCl (0.508 g, 1.31 mmol) in CH₂Cl₂ (40 mL) was stirred and refluxed for 6 hours. The mixture was cooled to room temperature, diluted to 190 mL with CH₂Cl₂, washed with saturated NH₄Cl solution (3 X 40 mL), and dried (MgSO₄). Solvent was evaporated from the CH₂Cl₂ solution and the product was purified by flash column chromatography on silica gel using CHCl₃/MeOH/2M NH₃ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.487 g, 60.5%); mp 99-101 °C. Anal. Calcd for C₃₃H₃₈N₆O₆·0.55 CH₂Cl₂: C, 60.93; H, 5.96; N, 12.71. Found: C, 60.94; H, 5.77; N, 12.66.

15

EXAMPLE 210

5-Carboxamido-3-{N-[3-(4-carboxy-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine (210). a stirred solution of 5-carboxamido-3-{N-[3-(4-(2-cyanoethoxycarbonyl)-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine (0.394 g, 0.641 mmol) in dioxane (2 mL) at 0 °C, aqueous 1N sodium hydroxide (1.92 mL, 1.92 mmol) was added and the mixture was allowed to warm to room temperature. TLC analysis of the reaction mixture showed the completion of the reaction after 2 hours. Solvent was evaporated from the reaction mixture and the residue was redissolved in water (1 mL) and the pH was adjusted to 5-6 by the addition of 1N HCl. The brown precipitate formed was filtered and dried under vacuum (0.252 g, 70%); mp 208-210 °C. Anal. Calcd for C₃₀H₃₅N₅O₆·0.43 NaCl·1.0 H₂O: C, 59.57; H, 6.17; N, 11.58. Found: C, 59.57; H, 6.17; N, 11.48.

EXAMPLE 211

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5-Carboxamido-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-(2-methoxyethoxy)-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (211). A mixture of 5-carboxamido-3-{N-[3-(4-carboxy-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine (0.080 g, 0.142 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.0546 g, 0.284 mmol), 4-(N,N-dimethylamino)pyridine (0.0347 g, 0.284 mmol), and 2-methoxyethanol (0.0324 g, 0.426 mmol) in CH_2Cl_2 (15 mL) was stirred and refluxed for 14 hours and cooled. The reaction mixture was diluted to 50 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 10 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.032 g, 36%); mp 79-80 °C. Anal. Calcd for $\text{C}_{33}\text{H}_{41}\text{N}_5\text{O}_7$: C, 63.96; H, 6.67; N, 11.30. Found: C, 64.23; H, 6.45; N, 11.03.

EXAMPLE 212

5-Carboxamido-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-(2-hydroxyethoxy)-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (212). A mixture of 5-carboxamido-3-{N-[3-(4-carboxy-4-phenylpiperidin-1-yl)propyl]}carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine (0.055 g, 0.098 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.0375 g, 0.196 mmol), 4-(N,N-dimethylamino)pyridine (0.024 g, 0.196 mmol), and ethylene glycol (0.0182 g, 0.294 mmol) in CH_2Cl_2 (15 mL) was stirred and refluxed for 14 hours and cooled. The reaction mixture was diluted to 50 mL with CH_2Cl_2 , washed with saturated NH_4Cl solution (3 X 10 mL), and dried (MgSO_4). Solvent was evaporated from the CH_2Cl_2 solution

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and the product was purified by flash column chromatography on silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:4:2) as the eluent to afford the product as a yellow powder (0.038 g, 64%); mp 116-118 °C. Anal. Calcd for $\text{C}_{32}\text{H}_{39}\text{N}_5\text{O}_7 \cdot 0.6 \text{ CHCl}_3$: C, 57.81; H, 5.89; N, 10.34. Found: C, 57.68; H, 5.93; N, 10.23.

EXAMPLE 213

10 5-Carboxamido-1,4-dihydro-2,6-dimethyl-3-{N-[3-(4-phenoxy-4-phenylpiperidin-1-yl)propyl]}carboxamido-4-(4-nitrophenyl)pyridine (213). A mixture of
5 - c a r b o x a m i d o - 3 - { N - [3 -
(4-carboxy-4-phenylpiperidin-1-yl)propyl]}carbox-
15 amido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine
(0.050 g, 0.098 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.0375 g, 0.196 mmol),
4-(N,N-dimethylamino)pyridine (0.024 g, 0.196 mmol), and
phenol (0.028 g, 0.294 mmol) in CH_2Cl_2 (15 mL) was stirred
20 and refluxed for 14 hours and cooled. The reaction
mixture was diluted to 50 mL with CH_2Cl_2 , washed with
saturated NH_4Cl solution (3 X 10 mL), and dried (MgSO_4).
Solvent was evaporated from the CH_2Cl_2 solution and the
product was purified by flash column chromatography on
25 silica gel using $\text{CHCl}_3/\text{MeOH}/2\text{M NH}_3$ in MeOH (100:4:2) as
the eluent to afford the product as a yellow powder
(0.048 g, 77%); mp 121-122 °C. Anal. Calcd for
 $\text{C}_{36}\text{H}_{39}\text{N}_5\text{O}_6 \cdot 0.35 \text{ CHCl}_3$: C, 64.25; H, 5.84; N, 10.31. Found:
C, 64.10; H, 5.86; N, 10.07.

30

EXAMPLE 214

2-((2-Azidoethyl)oxy)methyl-5-carboxamido-3-(N-(3-(4-
c y a n o -
35 4-phenylpiperidin-1-yl)propyl))carboxamido-1,4-dihydro-
6-methyl-4-(4-nitrophenyl)pyridine 2-(4-
Nitrophenyl)methylene-3-oxo-1-butanamide: A mixture of 4-

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nitrobenzaldehyde (15.1 g, 100 mmol), acetoacetamide (10.1 g, 100 mmol), piperidine (0.852 g, 10 mmol), and HOAc (0.601 g, 10 mmol) in 250 mL of isopropanol were stirred at room temperature for 13 hours. The precipitated product was filtered, washed with 50 mL of isopropanol and 2 X 50 mL of ether, and air dried to give 20.1 g (86%) of the desired product as a slightly yellow solid: mp 148-155 °C. The product was used in the next step after spectral characterization.

10

2-((2-Azidoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic Acid: A mixture of 5-((2-azidoethyl)oxy)acetyl-2,2-dimethyl-4,6-dione-1,3-dioxane (7.24 g, 26.7 mmol) and 3-hydroxypropionitrile (3.80 g, 53.4 mmol) in 50 mL of dry toluene were heated at reflux temperature for 2 hours, cooled, and the solvent was removed in vacuo. The residue was charged with ammonium acetate (2.26 g, 29.4 mmol) and ethanol (50 mL) and heated at reflux temperature for 0.5 hour. 2-(4-Nitrophenyl)methylene-3-oxo-1-butanamide (4.38 g, 18.7 mmol) was added to the reaction mixture and heated at reflux temperature for 3 hours, cooled to room temperature, NaOH (139 mg), in 10 mL of water was added to the reaction mixture, and stirred for 3 hours. The solvent was removed in vacuo, the residue was partitioned between water (50 mL) and EtOAc (50 mL), separated, extracted with 2 X 50 mL of water, the combined aqueous extracts were acidified with concentrated HCl (pH = 3-4), extracted with dichloromethane (3 X 50 mL), dried (Na₂SO₄), and the solvent was removed in vacuo. The crude product was precipitated from a mixture of EtOAc-hexane to give 1.15 g of the desired acid as a yellow solid: mp 160-165 °C. The product was used in the next step after spectral characterization.

2-((2-Azidoethyl)oxy)methyl-5-carboxamido-3-(N-(3-(4-

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c y a n o -
 4-phenylpiperidin-1-yl)propyl))carboxamido-1,4-dihydro-
 6-methyl-4-(4-nitro)phenylpyridine (214): A mixture of 2-
 (2-azidoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-
 5 methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid 150
 mg, 0.373 mmol), DCC (154 mg, 0.746 mmol), DMAP (36 mg,
 0.300 mmol), and 1-(3-amino)propyl-4-cyano-
 4-phenylpiperidine (110 mg, 0.450 mmol) in 7 mL of dry
 dichloromethane were stirred at reflux temperature for 3
 10 hours. The solvent was removed in vacuo, redissolved in
 10 mL of ethyl acetate, filtered, solvent removed in
 vacuo, and the residue was chromatographed on 300 g of
 silica packed with MeOH-EtOAc (1:9). The column was
 eluted with MeOH-EtOAc (1:9) to give 133 mg (60%) of the
 15 desired product as a yellow solid: mp 81 °C (decomp.);
 Anal. Calcd for $C_{32}H_{37}N_9O_5 + 0.2CHCl_3$: C, 59.36; H, 5.75; N,
 19.35. Found: C, 59.74; H, 5.69; N, 19.08

EXAMPLE 215

20 2-((2-Aminoethyl)oxy)methyl-5-carboxamido-3-(N-(3-
 (4 - c y a n o -
 4-phenylpiperidin-1-yl)propyl))carboxamido-1,4-dihydro-
 6-methyl-4-(4-nitrophenyl)pyridine (215): To a solution
 25 of 2-((2-azidoethyl)oxy)methyl-5-carboxamido-3-(N-(3-
 (4 - c y a n o - 4 - p h e n y l -
 piperidin-1-yl)propyl))carboxamido-1,4-dihydro-6-methyl
 -4-(4-nitro)phenylpyridine (100 mg, 0.160 mmol) in 5 mL
 of EtOAc at 0 °C was added 1 M (Me)₃P in THF (0.40 mL,
 30 0.40 mmol), and water (14 mL, 0.80 mmol). The reaction
 mixture was stirred at room temperature for 3 hours, and
 the solvent was removed in vacuo. The crude product was
 chromatographed on 100 g of silica packed with NH₃ (2N in
 MeOH)-MeOH-CHCl₃ (1:2:10). The column was eluted with NH₃
 35 (2N in MeOH)-MeOH-CHCl₃ (1:2:10) to give 77 mg (80%) of
 the desired product as a yellow solid: mp 101 °C
 (decomp.); Anal. Calcd for $C_{38}H_{45}N_5O_6 + 0.5CH_2Cl_2$: C, 60.60;

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H, 6.26; N, 15.22. Found: C, 60.65; H, 6.12; N, 15.37.

EXAMPLE 216

5 2-((Azidoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4-phenylpiperidin-1-yl)propyl))carboxamidopyridine (216): A mixture of 2-(2-azidoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (150 mg,
10 0.373 mmol), DCC (154 mg, 0.746 mmol), DMAP (36 mg, 0.300 mmol), and 1-(3-amino)propyl-4-phenylpiperidine (87 mg, 0.400 mmol) in 7 mL of dry dichloromethane were stirred at reflux temperature for 4 hours, and then at room temperature for 17 hours. The solvent was removed in
15 vacuo, redissolved in 10 mL of ethyl acetate, filtered, washed with aqueous saturated ammonium chloride solution (3 X 3 mL), brine (3 mL), dried (Na₂SO₄), solvent removed in vacuo, and the residue was chromatographed on 300 g of silica packed with MeOH-EtOAc (1:3). The column was
20 eluted with MeOH-EtOAc (1:3) to give 133 mg (60%) of the desired product as a yellow solid: mp 76 °C (decomp.); Anal. Calcd for C₃₂H₃₇N₅O₅+0.12CHCl₃: C, 60.58; H, 6.23; N, 18.16. Found: C, 60.76; H, 6.22; N, 17.76.

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EXAMPLE 217

2-((2-Aminoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-methyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (217): To a solution of 2-((2-aminoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-methyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (116 mg, 0.170 mmol) in 5 mL of EtOAc
30 at 0 °C was added 1 M (Me)₃P in THF (0.43 mL, 0.43 mmol), stirred at 0 °C for 10 minutes, and water (15 mL, 0.85 mmol) was added. The reaction mixture was stirred at
35

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room temperature for 2 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 150 g of silica packed with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:10). The column was eluted with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:10) to give 88 mg (80%) of the desired product as a yellow solid: mp 130-140 °C; Anal. Calcd for $\text{C}_{38}\text{H}_{45}\text{N}_5\text{O}_6 + 0.7\text{CH}_2\text{Cl}_2$: C, 63.58; H, 6.42; N, 11.80. Found: C, 63.56; H, 6.62; N, 11.55.

10

EXAMPLE 218

2-((2-Aminoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4-phenylpiperidin-1-yl)propyl))carboxamidopyridine (218): To a solution of 2-((2-(azidoethyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4-phenylpiperidin-1-yl)propyl))carboxamidopyridine (88 mg, 0.146 mmol) in 6 mL of EtOAc at 0 °C was added 1 M $(\text{Me})_3\text{P}$ in THF (0.37 mL, 0.37 mmol), and water (13 mL, 0.73 mmol) was added. After 15 minutes, a precipitate was formed which redissolved after addition of 4.5 mL of dry THF. The reaction mixture was stirred at room temperature for 4 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 140 g of silica packed with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:10). The column was eluted with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:10) to give 65 mg (80%) of the desired product as a yellow solid: mp 125 °C (decomp.); Anal. Calcd for $\text{C}_{38}\text{H}_{45}\text{N}_5\text{O}_6 + 0.35\text{CH}_2\text{Cl}_2$: C, 62.09; H, 6.76; N, 13.86. Found: C, 62.22; H, 6.88; N, 13.51.

EXAMPLE 219

2-((2-Aminoethyl)oxy)methyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-carboxylic Acid (219):
T o a s o l u t i o n o f

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- 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-carboxylic acid (38 mg, 0.055 mmol) in 4 mL of THF-EtOAc (1:3) at 0 °C was added
- 5 1 M (Me)₃P in THF (0.14 mL, 0.14 mmol), and water (12 mL, 0.67 mmol). The reaction mixture was stirred at room temperature for 2 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 75 g of silica packed with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:7).
- 10 The column was eluted with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:7) to give 30 mg (82%) of the desired product as a yellow solid. The chromatographed contained small amounts of an impurity. The product was precipitated from a mixture of EtOH-EtOAc: mp 180 °C (decomp.); Anal.
- 15 Calcd for C₃₈H₄₅N₅O₆+1.4H₂O+0.7CHCl₃: C, 59.86; H, 6.29; N, 9.02. Found: C, 59.89; H, 6.09; N, 8.77.

EXAMPLE 220

- 20 5-(2-Cyanoethoxy)carbonyl-3-(N-(3-(4-cyano-4-phenylpiperidin-1-yl)propyl))carboxamido-6-ethyl-1,4-dihydro-2-methyloxymethyl-4-(4-nitro)phenylpyridine (220): A mixture of 5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-methyloxymethyl-4-(4-nitro)phenylpyridine-3-carboxylic
- 25 acid (150 mg, 0.361 mmol), DCC (149 mg, 0.722 mmol), and DMAP (35 mg, 0.289 mmol) in 12 mL of dry dichloromethane were stirred at room temperature for 1 hour before addition of 1-(3-amino)propyl-4-cyano-4-phenylpiperidine (114 mg, 0.469 mmol). The resulting mixture was heated
- 30 at reflux temperature for 3 hours. The reaction mixture was filtered, concentrated in vacuo, and the residue was chromatographed on 300 g of silica (MeOH-EtOAc, 1:29) to give 196 mg of the title compound (85%) as a yellow solid: mp 58-68 °C; Anal Calcd for C₃₅H₄₀N₆O₆+0.7H₂O: C,
- 35 64.34; H, 6.39; N, 12.86. Found: C, 64.69; H, 6.50; N, 12.49.

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EXAMPLE 221

5-(2-Cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-methyloxymethyl-4-(4-nitro)phenyl-3-(N-(3-(4-phenylpiperidin-1-yl)propyl))carboxamidopyridine (221): A mixture of 5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-2-methyloxymethyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (150 mg, 0.361 mmol), DCC (149 mg, 0.722 mmol), and DMAP (35 mg, 0.289 mmol) in 8 mL of dry dichloromethane were stirred at room temperature for 0.5 hour before addition of 1-(3-amino)propyl-4-phenylpiperidine (103 mg, 0.469 mmol). The resulting mixture was heated at reflux temperature for 2.5 hours. The reaction mixture was filtered, concentrated in vacuo, and the residue was chromatographed on 120 g of silica (MeOH-EtOAc, 1:9) to give 200 mg of the title compound (90%) as a yellow solid: mp 55-63 °C; Anal. Calcd for $C_{34}H_{41}N_5O_6 + 0.5H_2O$: C, 65.37; H, 6.78; N, 11.21. Found: C, 65.23; H, 6.77; N, 10.94.

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EXAMPLE 222

3-(N-(3-(4-Cyano-4-phenylpiperidin-1-yl)propyl))carboxamido-6-ethyl-1,4-dihydro-2-methyloxymethyl-4-(4-nitro)phenylpyridine-5-carboxylic Acid (222): To a solution of 3-(N-(3-(4-cyano-4-phenylpiperidin-1-yl)propyl))carboxamido-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenyl-2-methyloxymethylpyridine (170 mg, 0.265 mmol) in 3 mL of dioxane was added water containing NaOH (16 mg, 0.398 mmol). After 2 hours, the solvent was removed in vacuo, the residue was dissolved in water (20 mL), acidified with aqueous 1 N HCl solution (pH = 3-4), and extracted with dichloromethane (3 X 15 mL). The combined dichloromethane extracts were dried (Na_2SO_4), and the solvent was removed in vacuo to give 150 mg (96%) of the desired product as a yellow solid: mp 115 °C (decomp.):

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Anal. Calcd for $C_{32}H_{37}N_5O_6 + 1.0H_2O + 0.5CH_2Cl_2$: C, 60.23; H, 6.22; N, 10.81. Found: C, 60.35; H, 6.20; N, 10.76.

EXAMPLE 223

5
6-Ethyl-1,4-dihydro-2-methyloxymethyl-4-(4-nitro)phenyl-
3 - (N - (3 -
(4-phenylpiperidin-1-yl)propyl))carboxamidopyridine-5-
carboxylic Acid (223): To a solution of 5-(2-
10 cyanoethoxy)carbonyl-
6-ethyl-1,4-dihydro-2-methyloxymethyl-4-(4-nitro)phenyl-
3 - (N - (3 -
(4-phenylpiperidin-1-yl)propyl))carboxamidopyridine (110
mg, 0.180 mmol in 2 mL of dioxane was added 0.70 mL of
15 water containing NaOH (11 mg, 0.270 mmol). After 2.5
hours, the solvent was removed in vacuo, the residue was
dissolved in water (8 mL), acidified with aqueous 1 N HCl
solution (pH = 5), and extracted with dichloromethane (3
X 8 mL). The combined dichloromethane extracts were
20 dried (Na_2SO_4), and the solvent was removed in vacuo to
give 100 mg (100%) of the title compound as a yellow
solid: mp 88 °C (decomp.): Anal. Calcd for
 $C_{32}H_{37}N_5O_6 + 0.4CH_2Cl_2$: C, 63.21; H, 6.55; N, 9.39. Found: C,
63.21; H, 6.60; N, 8.92.

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EXAMPLE 224

2-((2-Azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-
5-N-methylcarboxamido-4-(4-nitro)phenyl-3-(N-(3-(4,4-
30 diphenylpiperidin-1-yl)propyl))carboxamidopyridine (224):
A mixture of 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-
dihydro-4-(4-nitro)phenyl-3-(N-(3-
(4,4-diphenylpiperidin-1-yl)propyl))
carboxamidopyridine-5-carboxylic acid (100 mg, 0.144
35 mmol), DCC (48 mg, 0.231 mmol), and DMAP (122 mg, 14.1
mmol) in 5 mL of dry dichloromethane were stirred at room
temperature for 1 hour followed by addition of 40%

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methylamine in water (0.123 mL, 1.44 mmol). The resulting mixture was stirred at room temperature for 18 hours. The reaction mixture was filtered, and the solvent was removed in vacuo. The crude product was dissolved in 10 mL of EtOAc, sequentially washed with aqueous saturated ammonium chloride (3 X 2 mL), water (2 mL), aqueous saturated sodium chloride solution (3 mL), dried (Na_2CO_3), and the solvent was removed in vacuo. The product was chromatographed on 100 g of silica packed with MeOH-EtOAc (1:4). The column was eluted with MeOH-EtOAc (1:4) to afford 88 mg (90%) of the desired product as a yellow solid: mp 95 °C (decomp.); Anal. Calcd for $\text{C}_{39}\text{H}_{46}\text{N}_8\text{O}_5 + 1.7\text{H}_2\text{O}$: C, 63.52; H, 6.75; N, 15.19. Found: C, 63.46; H, 6.32; N, 14.82.

EXAMPLE 225

2-((2-Aminoethyl)oxy)methyl-6-ethyl-1,4-dihydro-5-N-methylcarboxamido-4-(4-nitro)phenyl-3-(3-(N-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (225): To a solution of 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-5-N-methylcarboxamido-4-(4-nitro)phenyl-3-(3-(N-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (75 mg, 0.11 mmol) in 5 mL of EtOAc at 0 °C was added 1 M $(\text{Me})_3\text{P}$ in THF (0.44 mL, 0.44 mmol), and water (20 mL, 1.1 mmol). The reaction mixture was stirred at room temperature for 3 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:15). The column was eluted with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1 L of 1:2:17 and 1 L of 1:2:15) to give 60 mg (83%) of the desired product as a yellow solid: mp 115 °C (decomp.); Anal. Calcd for $\text{C}_{39}\text{H}_{48}\text{N}_6\text{O}_5 + 1.0\text{H}_2\text{O}$: C, 67.03; H, 7.21; N, 12.03. Found: C, 66.98; H, 7.18; N, 11.54.

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EXAMPLE 226

2-((2-Azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (226): A mixture of 2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-3-carboxylic acid (1.00 g, 2.13 mmol), DCC (877 mg, 4.25 mmol), and DMAP (208 mg, 1.70 mmol) in 40 mL of dry dichloromethane were stirred at room temperature for 15 minutes followed by addition of 1-(3-amino)propyl-4-methoxycarbonyl-4-phenylpiperidine (630 mg, 2.28 mmol). The resulting mixture was stirred at room temperature for 19 hours, filtered, and the solvent was removed in vacuo. The product was chromatographed on 750 g of silica packed with MeOH-EtOAc (1:9). The column was eluted with MeOH-EtOAc (1:9) to afford 1.33 g (84%) of the desired product as a yellow solid: mp 54-60 °C; Anal. Calcd for $C_{37}H_{44}N_8O_8$: C, 60.97; H, 6.10; N, 15.37. Found: C, 60.81; H, 6.24; N, 15.12.

EXAMPLE 227

2-((2-Azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine-5-carboxylic Acid (227): To a solution of 2-((2-azidoethyl)oxy)methyl-5-(2-cyanoethoxy)carbonyl-6-ethyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (1.30 g, 1.78 mmol) in 10 mL of dioxane was added NaOH (75 mg, 1.87 mmol) in 5 mL of water. The reaction mixture was stirred at room temperature for 2 hours, and the solvent was removed in vacuo. The residue was dissolved in 50 mL of water, acidified with 1 N HCl

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solution (pH = 5), the precipitated solids were filtered, and dried (MgSO_4) to give 1.20 g (100%) of the desired product as a yellow solid: mp 110-120 °C: Anal calcd for $\text{C}_{34}\text{H}_{41}\text{N}_7\text{O}_8 + 1.5\text{H}_2\text{O}$: C, 58.11; H, 6.31; N, 13.95. Found: C, 58.38; H, 5.99; N, 13.85.

EXAMPLE 228

2-((2-Azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(N-(3-
 10 (4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carbo
 xamido-5-N-methylcarboxamido-4-(4-nitro)phenylpyridine
 (2 2 8) : A s o l u t i o n o f
 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(N-(3-
 (4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carbo
 15 xamido-4-(4-nitro)phenylpyridine-5-carboxylic acid (100
 mg, 0.148 mmol), DCC (61 mg, 0.296 mmol), and DMAP (14
 mg, 0.118 mmol) in 4 mL of dry dichloromethane were
 stirred at room temperature for 0.5 hour, the reaction
 mixture was charged with 0.13 mL of 40% MeNH_2 in water,
 20 and stirred at room temperature for 16 hours. The
 reaction mixture was filtered, the solvent was removed in
 vacuo, and the crude product was chromatographed on 100
 g of silica packed with MeOH-EtOAc (1:6). The column was
 eluted with MeOH-EtOAc (1:6) to give 71 mg (70%) of the
 25 desired product as a yellow solid: mp 73-83 °C; Anal.
 Calcd for $\text{C}_{35}\text{H}_{44}\text{N}_8\text{O}_7 + 0.2\text{H}_2\text{O}$: C, 59.90; H, 6.34; N, 15.88.
 Found: C, 59.74; H, 6.50; N, 15.60

EXAMPLE 229

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2-((2-Aminoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(N-(3-
 (4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carbo
 xamido-5-N-methylcarboxamido-4-(4-nitro)phenylpyridine
 (2 2 9) : T o a s o l u t i o n o f
 35 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(N-(3-
 (4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carbo
 xamido-5-N-methylcarboxamido-4-(4-nitro)phenylpyridine

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(54 mg, 0.078 mmol) in 3 mL of EtOAc at 0 °C was added 1 M (Me)₃P in THF (0.30 mL, 0.30 mmol), and water (14 mL, 0.78 mmol). The reaction mixture was stirred at room temperature for 4 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:15). The column was eluted with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:15) to give 44 mg (85%) of the desired product as a yellow solid: mp 95 °C (decomp.); Anal. Calcd for C₃₅H₄₆N₆O₇+1.0H₂O: C, 61.75; H, 7.11; N, 12.34. Found: C, 61.74; H, 7.10; N, 12.02.

EXAMPLE 230

2-((2-Azidoethyl)oxy)methyl-6-ethyl-5-N-ethylcarboxamido-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (230): A solution of 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine-5-carboxylic acid (120 mg, 0.178 mmol), DCC (73 mg, 0.36 mmol), and DMAP (17 mg, 0.118 mmol) in 5 mL of dry dichloromethane were stirred at room temperature for 1.5 hours, the reaction mixture was charged with 0.144 mL of 70% EtNH₂ in water (1.78 mmol), and stirred at room temperature for 2 days. The reaction mixture was filtered, and the solvent was removed in vacuo. The crude product was dissolved in 10 mL of EtOAc, sequentially washed with aqueous saturated ammonium chloride (5 mL), water (5 mL), aqueous saturated sodium carbonate solution (5 mL), dried (Na₂CO₃), and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with MeOH-EtOAc (1:9). The column was eluted with MeOH-EtOAc (1:9) to give 50 mg (45%) of the desired product as a yellow solid: mp 70 °C (decomp.); Anal. Calcd for C₃₆H₄₆N₈O₇+1.0H₂O: C, 59.99; H, 6.71; N, 15.55. Found: C,

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60.02; H, 6.79; N, 14.56.

EXAMPLE 231

5 2-((2-Azidoethyl)oxy)methyl-5-carboxamido-6-ethyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (231):
 A m i x t u r e o f
 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(N-(3-
 10 (4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine-5-carboxylic acid (120 mg, 0.178 mmol), DCC (73 mg, 0.36 mmol), and DMAP (17 mg, 0.118 mmol) in 5 mL of dry dichloromethane were stirred at room temperature for 1.5 hours, the reaction mixture
 15 was charged with 1.78 mL of 58% NH₄OH in water (1.78 mmol), and stirred at room temperature for 2 days. The reaction mixture was filtered, the solvent was removed in vacuo. The crude product was dissolved in 10 mL of EtOAc, sequentially washed with aqueous saturated
 20 ammonium chloride (5 mL), water (5 mL), aqueous saturated sodium carbonate solution (5 mL), dried (Na₂CO₃), and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with MeOH-EtOAc (1:9). The column was eluted with MeOH-EtOAc (1:9) to
 25 give 50 mg (42%) of the desired product as a yellow solid: mp 70-75 °C; Anal. Calcd for C₃₄H₄₂N₈O₇+1.0H₂O: C, 58.95; H, 6.40; N, 16.17. Found: C, 58.86; H, 6.19; N, 15.81.

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EXAMPLE 232

2-((2-Azidoethyl)oxy)methyl-6-ethyl-5-methoxycarbonyl-3-
 - (N - (3 -
 (4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carbo
 35 xamido-1,4-dihydro-4-(4-nitro)phenylpyridine (232): A mixture of 2-((2-azidoethyl)oxy)methyl-6-ethyl-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperid-

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in-1-yl)propyl))carboxamido-1,4-dihydro-4-(4-nitro)phenylpyridine-5-carboxylic acid (120 mg, 0.178 mmol), DCC (73.3 mg, 0.353 mmol), and DMAP (17.4 mg, 0.142 mmol) in 5 mL of dry dichloromethane were stirred at room temperature for 2 hours, the reaction mixture was charged with methanol (72 mL, 9.6 mmol, 1.78 mmol), and stirred at room temperature for 2 days. The reaction mixture was filtered, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with MeOH-EtOAc (1:9). The column was eluted with MeOH-EtOAc (1:19) to give 91 mg (74%) of the desired product as a yellow solid: mp 50-60 °C; Anal. Calcd for $C_{35}H_{43}N_7O_8 + 0.5H_2O$: C, 60.16; H, 6.35; N, 14.03. Found: C, 60.33; H, 6.51; N, 13.84.

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EXAMPLE 233

2-((2-Aminoethyl)oxy)methyl-6-ethyl-5-N-ethylcarboxamido-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (233): To a solution of 2-((2-Azidoethyl)oxy)methyl-6-ethyl-5-N-ethylcarboxamido-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (30 mg, 0.043 mmol) in 4 mL of EtOAc at 0 °C was added 1 M $(Me)_3P$ in THF (0.17 mL, 0.17 mmol), and water (8 mL, 0.43 mmol). The reaction mixture was stirred at room temperature for 4 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with NH_3 (2N in MeOH)-MeOH- $CHCl_3$ (1:2:12). The column was eluted with NH_3 (2N in MeOH)-MeOH- $CHCl_3$ (1:2:12) to give 25 mg (86%) of the desired product as a yellow solid: mp 112 °C (decomp.); Anal. Calcd for $C_{36}H_{48}N_8O_7 + 0.5H_2O + 0.5CH_2Cl_2$: C, 60.20; H, 6.92; N, 11.54. Found: C, 60.14; H, 7.31; N, 11.23.

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EXAMPLE 234

2-((2-Aminoethyl)oxy)methyl-5-carboxamido-6-ethyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (234): To a solution of 2-((2-Azidoethyl)oxy)methyl-5-carboxamido-6-ethyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (30 mg, 0.044 mmol) in 4 mL of EtOAc at 0 °C was added 1 M (Me)₃P in THF (0.18 mL, 0.18 mmol), and water (16 mL, 0.88 mmol). The reaction mixture was stirred at room temperature for 4 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:15). The column was eluted with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:15) to give 44 mg (95%) of the desired product as a yellow solid: mp 115 °C (decomp.); Anal. Calcd for C₃₅H₄₆N₆O₇+1.0H₂O+0.2CH₂Cl₂: C, 60.08; H, 6.84; N, 12.29. Found: C, 60.37; H, 6.96; N, 11.98.

EXAMPLE 235

2-((2-Aminoethyl)oxy)methyl-6-ethyl-1,4-dihydro-5-methoxycarbonyl-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (235): To a solution of 2-((2-azidoethyl)oxy)methyl-6-ethyl-1,4-dihydro-5-methoxycarbonyl-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(4-nitro)phenylpyridine (65 mg, 0.094 mmol) in 4 mL of EtOAc at 0 °C was added 1 M (Me)₃P in THF (0.38 mL, 0.38 mmol), and water (34 mL, 1.88 mmol). The reaction mixture was stirred at room temperature for 2.5 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of

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silica packed with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:30). The column was eluted with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:15) to give 55 mg (88%) of the desired product as a yellow solid: mp 70 °C (decomp.).

5

The hydrochloride salt was prepared by dissolving 5 mg of 2-((2-aminoethyl)oxy)methyl-6-ethyl-1,4-dihydro-5-methoxycarbonyl-4-(4-nitro)phenylpyridine in 2 mL of dichloromethane and 2 mL of 1 N HCl in ether was added, the precipitated product was collected, and dried: mp 140 °C (decomp.); Anal. Calcd for $\text{C}_{35}\text{H}_{45}\text{N}_5\text{O}_8 + 2.0\text{HCl} + 1.5\text{H}_2\text{O}$: C, 55.05; H, 6.60; N, 9.17. Found: C, 54.80; H, 6.22; N, 8.58.

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EXAMPLE 236

5-Acetyl-2-((3-aminopropyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (236) 3-(4-Nitrophenyl)methylenepentane-2,4-dione: A mixture of pentane-2,4-dione (20.0 g, 200 mmol), 4-nitrobenzaldehyde (30.2 g, 200 mmol), piperidine (1.70 g, 20.0 mmol), and HOAc (1.20 g, 20.0 mmol) in 500 mL of isopropanol were heated with a heat gun until a homogeneous solution resulted. The reaction mixture was then stirred at room temperature for 18 hours. The precipitated solids were filtered, sequentially washed with isopropanol and ether, and air dried to give 28.3 g of the title compound. The filtrate also yielded 5.10 g of 3-(4-nitrophenyl)methylenopentane-2,4-dione for a combined yield of 72%: mp 90-91 °C. The product was used in the next step after spectral characterization.

35

3-Azidopropanol: A mixture of 3-chloropropanol (100 g, 1.06 mol), sodium azide (103 g, 1.59 mol), NaOH (636 mg,

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15.9 mol), and NaI (2.39 g, 15.9 mmol) in a mixture of H₂O-EtOH (2:1, 750 mL) were stirred at 60-65 °C (bath temperature) for 3 days. The reaction mixture was cooled, extracted with EtOAc (3 X 250 mL), dried (MgSO₄), and the solvent was removed in vacuo. The crude product was distilled under reduced pressure to give 98.6 g (92%) of 3-azidopropanol as a colorless oil: bp 56-58 (0.2 mmHg). The product was used in the next step after spectral characterization.

10

(3-Azidopropyl)oxyacetic Acid: A solution of 3-azidopropanol (70.1 g, 0.693 mol) in 100 mL of THF was added dropwise, in a period of 1.5 hours, to a mechanically stirred suspension of NaH (60% in mineral oil, 30.5 g, 0.763 mol) in 250 mL of THF. During the addition of 3-azidopropanol, a gentle reflux was maintained. This was followed by addition of solid NaI (10.4 g, 69.3 mmol), and tetrabutylammonium bromide (22.3 g, 69.3 mmol), and sodium chloroacetate (88.8 g, 0.763 mol). The reaction mixture was heated at reflux temperature for 19 hours, cooled, quenched initially with 20 mL of water (added dropwise) and then with 700 mL of water, washed with EtOAc (3 X 200 mL), acidified with concentrated HCl to pH = 2, and extracted with dichloromethane (6 X 100 mL). The combined dichloromethane extracts were dried (MgSO₄), and the solvent was removed in vacuo to give 63.3 g (58%) of the title compound as a yellow viscous oil. The crude product was used in the next step after spectral characterization.

5-((3-Azidopropyl)oxy)acetyl-2,2-dimethyl-4,6-dione-1,3-dioxane: Carbonyldiimidazole (71.7 g, 0.442 mol) was added portionwise to a stirred solution of (3-azidopropyl)oxyacetic acid (63.1 g, 0.402 mol) in 300 mL of dry dichloromethane (bubbling). The resulting mixture was stirred at room temperature for 2 hours. A solution

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of pyridine (35.8 mL, 0.442 mol) and Meldrum's acid (63.7 g, 0.442 mol) in 150 mL of dry dichloromethane were added, over a period of 2 hours to the reaction mixture (slightly exothermic reaction). The reaction mixture was stirred for 16 hours, quenched with 400 mL of 2 N HCl (bubbling), separated, washed sequentially with 2 X 400 mL 2 N HCl, brine (400 mL), dried (MgSO₄), and the solvent was removed in vacuo to give 83.2 g (73%) of the title compound as a yellow viscous oil. The crude product was used in the next step after spectral characterization.

2-Cyanoethyl 3-Amino-4-((3-azidopropyl)oxy)crotonate: A mixture of 5-((3-azidopropyl)oxy)acetyl-2,2-dimethyl-4,6-dione-1,3-dioxane (8.39 g, 29.4 mmol) and 3-hydroxypropionitrile (4.48 g, 63.0 mmol) in 25 mL of dry toluene were heated at reflux temperature for 1 hour. The solvent was removed in vacuo, the residue was charged with 35 mL of EtOH and 2.72 g of NH₄OAc (35.3 mmol) and heated at reflux temperature for 20 minutes. The crude reaction mixture was divided into aliquotes and used in the next step without any further purification or characterization.

5-Acetyl-2-((3-azidopropyl)oxy)methyl-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine: A solution of 2-cyanoethyl 3-Amino-4-((3-azidopropyl)oxy)crotonate (4.94 g, 19.6 mmol), 3-(4-nitrophenyl)methylenopentane-2,4-dione (4.57 g, 19.6 mmol) in 20 mL of EtOH were heated at reflux temperature for 2.5 hours. The solvent was removed in vacuo, and the crude product was chromatographed on 500 g of silica packed with 50% EtOAc-hexane. The column was eluted with increasing amounts of EtOAc (2 L/10% change) to give 7.21 g of the title compound. Spectral analysis showed the presence of impurities and 3-hydroxypropionitrile in the chromatographed product. This was used in the next deprotection step without any further purification.

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5-Acetyl-2-((3-azidopropyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic Acid: A solution of 5-acetyl-2-((3-azidopropyl)oxy)methyl-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine (7.21 g, containing impurities), NaOH (620 mg, 15.5 mmol) in a mixture of dioxane-water (75 mL, 2:1) were stirred at room temperature for 0.5 hours. The solvent was removed in vacuo, the residue was partitioned between water (50 mL) and EtOAc (50 mL), separated, and the EtOAc wash was extracted with water (2 X 20 mL). The combined water extracts were acidified with concentrated HCl (pH = 2-3). The precipitated oil solidified on standing. The solids were precipitated from MeOH-H₂O, filtered, and air dried to give 2.72 g (33% from the Meldrum's intermediate) of the title compound as a yellow solid: mp 100 °C (decomp.). The product was used in the next step after spectral characterization.

5-Acetyl-2-((3-azidopropyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine: A mixture of 5-acetyl-2-((3-azidopropyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (416 mg, 1.00 mmol), 1-(3-amino)propyl-4,4-diphenylpiperidine (353 mg, 1.2 mmol), DCC 619 mg, 3.00 mmol), and DMAP (134 mg, 1.10 mmol) in 15 mL of dry dichloromethane were stirred at room temperature for 2 days, diluted with 10 mL of EtOAc, filtered, and chromatographed on 400 g of silica packed with MeOH-EtOAc (1:10). The column was eluted with 1:10 (1 L), 1.5:10 (1 L), 2:10 (1 L), 2:8 (3 L), to give 410 mg (59%) of the title compound as a yellow solid: mp 72-80 °C; Anal. Calcd for C₃₉H₄₅N₇O₅+1.5H₂O: C, 65.16; H, 6.73; N, 13.64. Found: C, 65.23; H, 6.44; N, 13.70.

5 - A c e t y l - 2 - ((3 -
aminopropyl)oxy)methyl-1,4-dihydro-6-methyl-
4 - (4 - n i t r o) p h e n y l -

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- 3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine: To a solution of 5-acetyl-2-((3-azidopropyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine (338 mg, 0.489 mmol) in 20 mL of EtOAc at 0 °C was added 1 M (Me)₃P in THF (1.22 mL, 1.22 mmol), and water (88 mL, 4.89 mmol). The reaction mixture was stirred at room temperature for 2 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 350 g of silica packed with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:10). The column was eluted with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:10) to give 240 mg (75%) of the desired product as a yellow solid: mp 80 °C (decomp.); Anal. Calcd for C₃₆H₄₇N₅O₅+1.5H₂O: C, 67.61; H, 7.27; N, 10.11. Found: C, 67.23; H, 7.14; N, 10.01.

EXAMPLE 237

- 5-Acetyl-2-((2-aminoethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (237)
- 5-Acetyl-2-((2-azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid: A mixture of 5-((2-azidoethyl)oxy)acetyl-2,2-dimethyl-4,6-dione-1,3-dioxane (1.36 g, 5.00 mmol) and 3-hydroxypropionitrile (711 mg, 10.0 mmol) in 10 mL of dry toluene were heated at reflux temperature for 1 hour, and cooled. The residue was charged with EtOH (10 mL) and ammonium acetate (424 mg, 5.50 mmol), heated at reflux temperature for 0.5 hour, and cooled. The reaction mixture was charged with 3-(4-nitrophenyl)methylenopentane-2,4-dione (1.28 g, 5.50 mmol), and heated at reflux temperature for 2.5 hours, and cooled. Sodium hydroxide (1.00 g, 25.0

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mmol) in 5 mL of water was added to the reaction mixture and stirred at room temperature for 2 hours, and the solvent was removed in vacuo. To the residue was added water (10 mL), acidified with concentrated HCl (pH = 2-3), extracted with MeOH-CH₂Cl₂ (1:9, 5 X 50 mL), dried (MgSO₄), and the solvent was removed in vacuo. The crude product was chromatographed on 400 g of silica packed with EtOAc-hexane (1:1). The column was eluted with 80% EtOAc-hexane (2 L), EtOAc (2 L), MeOH-EtOAc (2 L) to give a product which contained many impurities. The product was partitioned between EtOAc (2 mL) and 0.05 N NaOH solution (2 mL), separated, and extracted with 3 X 2 mL 0.05 N NaOH solution. The combined aqueous extracts were acidified with concentrated HCl (pH = 2-3), extracted with 5 X 2 mL of dichloromethane, dried (Na₂SO₄), and the solvent was removed in vacuo to give 50 mg (3%) of the desired product as a yellow paste. The product was used in the next step without any further purification.

5 - A c e t y l - 2 - ((2 - azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine: A mixture of 5-acetyl-2-((2-azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (50 mg, 0.125 mmol), 1-(3-amino)propyl-4,4-diphenylpiperidine (44 mg, 0.149 mmol), DCC (77 mg, 0.373 mmol), and DMAP (17 mg, 0.137 mmol) in 2 mL of dry dichloromethane were stirred at room temperature for 2 days, filtered, and chromatographed on 100 g of silica packed with MeOH-EtOAc (1:9). The column was eluted with MeOH-EtOAc (10% to 20%, 1 L/5% change) to give 36 mg (41%) of the title compound as a yellow solid: mp 80-90 °C. The product was used in the next step after spectral characterization.

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5 - A c e t y l - 2 - ((2 - aminoethyl)oxy)methyl-1,4-dihydro-6-methyl-

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4 - (4 - n i t r o) p h e n y l -
 3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))
 carboxamidopyridine (237): To a solution of
 5 - a c e t y l - 2 - ((2 - a z i d o -
 ethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenyl-
 3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamido
 pyridine (32 mg, 0.047 mmol) in 3 mL of 1:1 THF-EtOAc at
 0 °C was added 1 M (Me)₃P in THF (0.118 mL, 0.118 mmol),
 and water (8.5 mL, 0.47 mmol). The reaction mixture was
 10 stirred at room temperature for 3 hours, and the solvent
 was removed in vacuo. The crude product was
 chromatographed on 100 g of silica packed with NH₃ (2N in
 MeOH)-MeOH-CHCl₃ (1:2:10). The column was eluted with NH₃
 (2N in MeOH)-MeOH-CHCl₃ (1:2:10) to give 10 mg (46%) of
 15 the desired product as a yellow solid: mp 100 °C
 (decomp.); Anal. Calcd for C₃H₄N₅O₅+0.5CHCl₃: C, 64.99; H,
 6.45; N, 9.84. Found: C, 64.81; H, 6.22; N, 9.92.

EXAMPLE 238

20

2-((3-Aminopropyl)oxy)methyl-5-carboxamido-1,4-dihydro-
 6-ethyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-dipheylpiperidin
 -1-
 yl)propyl))carboxamidopyridine (238)

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2-((3-Azidopropyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(2-
 trimethylsilylethoxy)carbonyl-4-(4-nitro)phenylpyridine-
 5-carboxylic Acid: A mixture of 5-((3-
 azidopropyl)oxy)acyl-2,2-dimethyl-4,6-dione-1,3-dioxane
 30 (33.8 g, 0.119 mol) and 2-trimethylsilylethanol (30.0 g,
 0.254 mol) in 100 mL of dry toluene were heated at reflux
 temperature for 1 hour. The reaction mixture was cooled,
 and the solvent was removed in vacuo. The residue was
 taken up in 100 mL of EtOH, ammonium acetate (11.0 g,
 35 0.142 mol) was added to the reaction mixture and heated
 at reflux temperature for 0.5 hour. The reaction mixture
 was divided into two aliquots and used in the next

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experiments. 2-Cyanoethyl 3-(4-nitrophenyl)methylene-3-oxopentanoate (17.0 g, 56.2 mmol) was added to one aliquot from above and heated at reflux temperature for 2.5 hours, and cooled. The solvent was removed in vacuo.

5 The oil was taken up in 50 mL of MeOH and water was added to oil out the product, which was taken up in 50 mL of dioxane and NaOH (2.61 g, 65.2 mmol) in 50 mL of water was added, stirred at room temperature for 0.5 hour, and the solvent was removed in vacuo. The residue was

10 partitioned between CH_2Cl_2 -EtOAc (1:2, 100 mL), and H_2O (50 mL), separated, and extracted with water (50 mL) and 3 X 50 mL of water containing 2.61 g of NaOH. The combined aqueous extracts were acidified with concentrated HCl (pH = 3-4), the precipitated oil was extracted with CHCl_3 -

15 EtOAc (2:1, 50 X 7 mL), the combined organic extracts were dried (MgSO_4) and the solvent was removed in vacuo. The crude product was chromatographed on 400 g of silica packed with EtOAc-hexane (1:4). The column was eluted with EtOAc-hexane (20%, 2 L; 30%, 1 L; 40%, 2 L) to

20 afford 5.60 g (18%) of the desired product as a yellow solid: mp 110 °C (decomp.). The product was used in the next step after spectral characterization.

2-((3-Azidopropyl)oxy)methyl-5-carboxamido-6-ethyl-1,4-

25 dihydro-3-(2-trimethylsilylethoxy)carbonyl-4-(4-nitro)phenylpyridine: A mixture of 2-((3-azidopropyl)oxy)methyl-6-ethyl-1,4-dihydro-3-(2-trimethylsilylethoxy)carbonyl-4-(4-nitro)phenylpyridine-5-carboxylic acid (390 mg, 0.734 mmol), DCC (227 mg, 1.10

30 mmol), and DMAP (99 mg, 0.807 mmol) in 2.5 mL of dry dichloromethane were stirred at room temperature for 1.5 hours. Ammonia (58%, 443 mg, 7.34 mmol) was added to the reaction mixture and stirred at room temperature 24

35 hours. The reaction mixture was filtered and chromatographed on 200 g of silica packed with MeOH-EtOAc-hexane (1:70:70). The column was eluted with the same solvent to afford 355 mg (91%) of the desired

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product as a yellow solid: mp 85-87 °C. The product was used in the next step after spectral characterization.

2-((3-Azidopropyl)oxy)methyl-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-3-carboxylic Acid: A solution of 3.24 mmol of tetrabutylammonium fluoride (1M) in 3.24 mL of THF was added, in one portion, to a stirred solution of 2-((3-azidopropyl)oxy)methyl-5-carboxamido-6-ethyl-1,4-dihydro-3-(2-trimethylsilylethoxy)carbonyl-4-(4-nitro)phenylpyridine (532 mg, 1.00 mmol) in 41 mL of DMSO. The resulting maroon solution was stirred at room temperature for 1 hour, poured into 50 mL of 1 N aqueous HCl solution, extracted with 50 mL and then with 3 X 20 mL of EtOAc. The combined EtOAc extracts were washed with water (3 X 20 mL), dried (Na₂SO₄), and the solvent was removed in vacuo. The crude product was chromatographed on 200 g of silica packed with 1% MeOH-EtOAc. The column was eluted with increasing amounts of MeOH (1% to 20%, 5%/2 L change) to give 160 mg (37%) of the desired product as a yellow solid: mp 138-143 °C. The product was used in the next step after spectral characterization.

2-((3-Azidopropyl)oxy)methyl-5-carboxamido-1,4-dihydro-6-ethyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)

propyl))carboxamidopyridine: A mixture of 2-((3-azido-propyl)oxy)methyl-5-carboxamido-6-ethyl-1,4-dihydro-4-(4-nitro)phenylpyridine-3-carboxylic acid (40 mg, 0.093 mmol), DCC (38 mg, 0.186 mmol), and DMAP (9 mg, 0.074 mmol) in 3 mL of dry dichloromethane were stirred at room temperature for 1 hour. The reaction mixture was charged with 1-(3-amino)propyl-4,4-diphenylpiperidine (34 mg, 0.12 mmol) and stirred at room temperature for 18 hours. The reaction mixture was filtered, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with MeOH-EtOAc (1:4). The

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column was eluted with the same solvent to afford 50 mg (76%) of the desired product as a yellow solid: mp 90-95 °C. The product was used in the next step after spectral characterization.

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2 - ((a z i d o p r o p y l) o x y) methyl-5-carboxamido-1,4-dihydro-6-ethyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (238): To a solution of
10 2 - ((a z i d o p r o p y l) o x y) methyl-5-carboxamido-1,4-dihydro-6-ethyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (45 mg, 0.064 mmol) in 3 mL of EtOAc at 0 °C
15 was added 1 M (Me)₃P in THF (0.16 mL, 0.16 mmol), and water (12 mL, 0.64 mmol). The reaction mixture was stirred at room temperature for 4 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:12). The column was eluted with 750
20 mL of NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:10) and 500 mL of NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:10) to give 30 mg (69%) of the desired product as a yellow solid: mp 92 °C (decomp.); Anal. Calcd for C₃₉H₄₈N₆O₅+0.8H₂O+0.8CH₂Cl₂: C, 62.64; H, 6.76; N, 11.09. Found: C, 62.39; H, 6.73; N, 11.19.

EXAMPLE 239

30 5-Acetyl-2-((2-aminoethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(3,4-methylenedioxy)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (239)
3-(3,4-Methylenedioxyphenyl)methylenepentane-2,4-dione: A mixture of pentane-2,4-dione (20.0 g, 200 mmol), 3,4-methylenedioxybenzaldehyde (32.2 g, 200 mmol), piperidine
35 (1.98 mL, 20.0 mmol), and HOAc (1.20 mL, 20.0 mmol) in 200 mL of isopropanol were stirred at room temperature

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for 3 days (no precipitate). The solvent was removed in vacuo, and the crude product was heated to 50-70 °C under reduced pressure for 0.5 hours (no solids). The crude product was chromatographed on 900 g of silica packed with 10% EtOAc-hexane. The column was eluted with increasing amounts of EtOAc (10% to 30%, 2.5%/2 L change) to give 19.1 g (41%) of the desired product as a yellow solid: mp 79-80 °C. The product was used in the next step after spectral characterization.

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5-Acetyl-2-((2-azidoethyl)oxy)methyl-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(3,4-methylenedioxy)phenylpyridine: A mixture of 5-((2-azidoethyl)oxy)acetyl-2,2-dimethyl-4,6-dione-1,3-dioxane (80%, 1.50 g, 4.42 mmol) and 3-hydroxypropionitrile (629 mg, 8.85 mmol) in 10 mL of dry toluene were heated at reflux temperature for 1.5 hours. The reaction mixture was cooled, and the solvent was removed in vacuo. The crude product was charged with ammonium acetate (477 mg, 6.19 mmol) and 10 mL of ethanol and heated at reflux temperature for 0.5 hour. and cooled to room temperature. The reaction mixture was charged with 3-(3,4-methylenedioxyphenyl)methylenopentane-2,4-dione (1.44 g, 6.19 mmol) and heated at reflux temperature for 5 hours. The solvent was removed in vacuo, and the crude product was chromatographed on 750 g of silica. The column was eluted with EtOAc-hexane (1:4, 2 L; 1:3, 2 L; 1:2, 2 L; 1:1, 2 L; 2:1, 2 L) to give 353 mg of spectroscopically pure and 200 mg of slightly impure product for a combined yield of 25% as a yellow paste. The crude product was used in the next deprotection step after spectral characterization.

5-Acetyl-2-((2-azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(3,4-methylenedioxy)phenylpyridine-3-carboxylic Acid: This product was obtained from deprotection of two batches of 5-acetyl-2-((2-azidoethyl)oxy)methyl-3-(2-

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cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(3,4-methylenedioxy)phenylpyridine obtained from the previous experiment (340 mg and 200 mg) and were combined after completion of the reaction. A mixture of 5-acetyl-2-((2-azidoethyl)oxy)methyl-3-(2-cyanoethoxy)carbonyl-1,4-dihydro-6-methyl-4-(3,4-methylenedioxy)phenylpyridine (340 mg, 0.750 mmol; 200 mg (60%), 0.200 mmol), 1 N NaOH (1.12 mL; 0.40 mL) in a mixture of dioxane (3 mL; 3 mL) were stirred at room temperature for 1.5 hours. The two batches were concentrated in vacuo, the combined batches were dissolved in 40 mL of water, washed with dichloromethane (30 mL) and EtOAc (20 mL), acidified with 1 N HCl solution (pH = 4-5), and extracted with dichloromethane (2 X 50 mL). The combined dichloromethane extracts were washed with brine (40 mL), dried (MgSO₄), and the solvent was removed in vacuo to give 300 mg (25%) of the title compound as a yellow paste which solidified on standing: mp 120 °C (decomp.). The product was used in the next step after spectral characterization.

5-Acetyl-2-((2-azidoethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(3,4-methylenedioxy)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine: A solution of 5-acetyl-2-((2-azidoethyl)oxy)methyl-4-(3,4-methylenedioxy)phenyl-1,4-dihydro-6-methylpyridine-3-carboxylic acid (60 mg, 0.150 mmol), DCC (62 mg, 0.300 mmol), and DMAP (15 mg, 0.120 mmol) in 3 mL of dry dichloromethane were stirred at room temperature for 20 minutes. The reaction mixture was charged with 1-(3-amino)propyl-4,4-diphenylpiperidine (53 mg, 0.180 mmol) and the reaction mixture was stirred at room temperature for 16 hours. The reaction mixture was filtered, and the solvent was removed in vacuo. The crude product was chromatographed on 300 g of silica packed with MeOH-EtOAc (1:9). The column was eluted with

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MeOH-EtOAc (1:9, 1.5 L; 1:4, 1 L) to give 82 mg (81%) of the title compound as a yellow solid: mp 75 °C (decomp.); Anal. Calcd for $C_{39}H_{44}N_6O_5 + 0.3H_2O + 0.3CH_2Cl_2$: C, 66.70; H, 6.44; N, 11.88. Found: C, 66.45; H, 6.15; N, 11.80.

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 5-Acetyl-2-((2-aminoethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(3,4-methylenedioxy)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (239): To a solution of 5-acetyl-2-((2-azidoethyl)oxy)methyl-4-(3,4-methylenedioxy)phenyl-1,4-dihydro-6-methyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (66 mg, 0.098 mmol) in 3 mL of EtOAc at 0 °C was added 1 M (Me)₃P in THF (0.30 mL, 0.29 mmol), and water (18 mL, 0.98 mmol). The reaction
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 15 mixture was stirred at room temperature for 4 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 130 g of silica packed with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:12). The column was eluted with 750 mL of NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:12) and 500 mL of
 20 NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:10) to give 52 mg (82%) of the desired product as a yellow solid: mp 80 °C (decomp.); Anal. Calcd for $C_{39}H_{46}N_4O_5 + 0.5H_2O + 0.5CH_2Cl_2$: C, 67.56; H, 6.89; N, 7.98. Found: C, 67.24; H, 6.85; N, 8.17.

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EXAMPLE 240

3-(N-3(4-Ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl)carboxamido-6-ethyl-1,4-dihydro-2-(methyloxy)methyl-
 30 4-(4-nitro)phenylpyridine-5-carboxylic Acid (240)

5-(2-Cyanoethoxy)carbonyl-3-(N-3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl)carboxamido-6-ethyl-1,4-dihydro-2-(methyloxy)methyl-4-(4-ni-
 35 tro)phenylpyridine: A mixture of 35 mg of 5-(2-

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cyanoethoxy) carbonyl-6-ethyl-1,4-dihydro-2-(methoxy)methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (0.084 mmol), 35 mg of DCC (0.169 mmol), and 8.2 mg of DMAP (0.067 mmol) in 3 mL of dry dichloromethane were stirred at room temperature for 1 hour before addition of 32 mg of 1-(3-amino)propyl-4-ethoxycarbonyl-4-phenylpiperidine (0.109 mmol). The resulting mixture was stirred at room temperature for 16 hours. The reaction mixture was concentrated in vacuo, and the residue was chromatographed on 180 g of silica (MeOH-EtOAc, 1:9) to give 40 mg of the title compound as a yellow solid (70%): mp 55 °C (decomp.). The product was used in the next step after spectral characterization.

3-(N-3-(4-Ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl)carboxamido-6-ethyl-1,4-dihydro-2-(methoxy)methyl-4-(4-nitro)phenylpyridine-5-carboxylic Acid (240) : To a solution of 5-(2-cyanoethoxy)carbonyl-3-(N-3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl)carboxamido-6-ethyl-1,4-dihydro-2-(methoxy)methyl-4-(4-nitro)phenylpyridine (35 mg, 0.051 mmol) in 3 mL of dioxane was added aqueous 1 M NaOH (56 mL, 0.056 mmol). After 1 hour, another equivalent of NaOH was added to the reaction mixture and stirred for 1.5 hours. The solvent was removed in vacuo, the residue was dissolved in water (8 mL), washed with dichloromethane (3 mL), and ethyl acetate (3 mL). The aqueous extract was acidified with aqueous 1 N HCl solution (pH = 3), and extracted with dichloromethane (3 X 15 mL). The combined dichloromethane extracts were dried (MgSO₄), and the solvent was removed in vacuo to give 11 mg (34%) of the title compound as a yellow solid: mp 116-126 °C; Anal. Calcd for C₃₄H₄₂N₄O₈+0.8EtOAc+0.4CH₂Cl₂: C, 61.10; H, 6.71; N, 7.58. Found: C, 61.02; H, 6.95; N, 7.26.

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EXAMPLE 241

5-Acetyl-2-((3-aminopropyl)oxy)methyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-6-methyl-4-(4-nitro)phenylpyridine (241)

5-Acetyl-2-((3-azidopropyl)oxy)methyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-6-methyl-4-(4-nitro)phenylpyridine: A mixture of 5-acetyl-2-((3-azidopropyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (115 mg, .278 mmol), and DMAP (27 mg, 0.222 mmol) in 10 mL of dry dichloromethane were stirred at room temperature for 2 hours. N-3-Aminopropyl-4-methoxycarbonyl-4-phenylpiperidine (100 mg, 0.362 mmol) was added to the reaction mixture and stirred at room temperature for 2 days. The reaction mixture was filtered, solvent was removed in vacuo, and the crude product was chromatographed on 350 g of silica packed with MeOH-EtOAc (1:9). The column was eluted with the same solvent to give 124 mg (66%) of the title compound as a yellow solid: mp 54 °C (decomp.); Anal. Calcd for $C_{35}H_{43}N_7O_7$: C, 62.38; H, 6.45; N, 14.54. Found: C, 61.93; H, 6.54; N, 14.19.

5-Acetyl-2-((3-aminopropyl)oxy)methyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-6-methyl-4-(4-nitro)phenylpyridine (241): To a solution of 5-acetyl-2-((azidopropyl)oxy)methyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-6-methyl-4-(4-nitro)phenylpyridine (95 mg, 0.141 mmol) in 4 mL of EtOAc at 0 °C was added 1 M $(Me)_3P$ in THF (0.36 mL, 0.35 mmol), and water (25 mL, 1.41 mmol). The

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reaction mixture was stirred at room temperature for 5 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:12). The column was
5 eluted with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:12) to give 72 mg (79%) of the desired product as a yellow solid: mp 70 °C (decomp.); Anal. Calcd for $\text{C}_{35}\text{H}_{45}\text{N}_5\text{O}_7 + 1.0\text{H}_2\text{O} + 0.1\text{CH}_2\text{Cl}_2$: C, 62.52; H, 7.06; N, 10.39. Found: C, 62.61; H, 6.96; N, 10.34.

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EXAMPLE 242

5-Acetyl-2-((2-aminoethyl)oxy)methyl-4-(4-fluoro)phenyl
-1,4-dihydro-6-methyl-3-(N-(3-(4,4-diphenylpiperidin-1-
15 yl)propyl))carboxamidopyridine (242)

3-(4-Fluorophenyl)methylenopentane-2,4-dione: A mixture of pentane-2,4-dione (20.0 g, 200 mmol), 4-fluorobenzaldehyde (24.8 g, 200 mmol), piperidine (1.95
20 mL, 20.0 mmol), and HOAc (1.20 mL, 20.0 mmol) in 100 mL of isopropanol were heated at reflux temperature for 5 minutes, and then at room temperature for 24 hours. The reaction mixture was cooled to -78 °C, filtered, and the solids were recrystallized from a mixture of CH_2Cl_2 -hexane
25 to give 35.2 g of 3-(4-fluorophenyl)methylenopentane-2,4-dione as a yellow crystalline solid: mp 34-35 °C; Anal. Calcd for $\text{C}_{12}\text{H}_{11}\text{F}_2\text{O}_2$: C, 69.89; H, 5.38. Found: C, 69.70; H, 5.38.

30 5-Acetyl-2-((2-azidoethyl)oxy)methyl-3-(2-cyanoethoxy)carbonyl-4-(4-fluoro)phenyl-1,4-dihydro-6-methylpyridine: A mixture of 5-((2-azidoethyl)oxy)acetyl-2,2-dimethyl-4,6-dione-1,3-dioxane (1.29 g, 3.54 mmol), 3-hydroxypropionitrile (503 mg, 7.08 mmol) in 10 mL of
35 dry toluene were heated at reflux temperature for 1.5 hours. The solvent was removed in vacuo, and the residue was dissolved in 10 mL of ethanol followed by addition of

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ammonium acetate (382 mg, 4.96 mmol). The reaction mixture was heated at reflux temperature for 1.5 hours, cooled, 3-(4-fluorophenyl)methylenopentane-2,4-dione (1.0 g, 4.96 mmol) was added to the reaction mixture, and
5 heated at reflux temperature for 4 hours. Additional 3-(4-fluorophenyl)methylenopentane-2,4-dione (0.4 g) was added to the reaction mixture and heated at reflux temperature for 3 hours. The solvent was removed in vacuo, and the crude product was chromatographed on 300
10 g of silica. The column was eluted with EtOAc-hexane (1:2.5, 1 L; 1:2, 2 L; and 1:1, 0.5 L) to give 520 mg of the title compound (48%) as a yellow paste. The product was used in the next step after spectral characterization.

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5-Acetyl-2-((2-azidoethyl)oxy)methyl-4-(4-fluoro)phenyl-1,4-dihydro-6-methylpyridine-3-carboxylic Acid: A mixture of 5-acetyl-2-((azidoethyl)oxy)methyl-3-(2-cyanoethoxy)carbonyl-4-(4-fluoro)phenyl-1,4-dihydro-6-
20 methylpyridine (500 mg, 1.17 mmol), 1.76 mL of 1 N NaOH solution (1.76 mmol), and 4 mL of dioxane were stirred at room temperature for 2 hours. The solvent was removed in vacuo, the residue dissolved in 30 mL of water, washed with 2 X 15 mL of dichloromethane, 10 mL of EtOAc,
25 acidified with 1 N HCl solution (pH = 4), and extracted with 3 X 25 mL of dichloromethane. The combined dichloromethane extracts were dried (Na₂SO₄), and the solvent was removed in vacuo to give 255 mg of the desired acid (40%) as a yellow solid: mp 100 °C (decomp.).
30 The product was used in the next step after spectral characterization.

5-Acetyl-2-((2-azidoethyl)oxy)methyl-4-(4-fluoro)phenyl-1,4-dihydro-6-methyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine:
35 A solution of 5-acetyl-2-((2-azidoethyl)oxy)methyl-4-(4-fluoro)phenyl-1,4-dihydro-6-methylpyridine-3-carboxylic

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acid (60 mg, 0.161 mmol), DCC (66 mg, 0.321 mmol), and DMAP (16 mg, 0.129 mmol) in 4 mL of dry dichloromethane were stirred at room temperature for 2 hours followed by addition of 1-(3-amino)propyl-4,4-diphenylpiperidine
 5 (56.9 mg, 0.193 mmol). The resulting mixture was stirred at room temperature for 18 hours. The reaction mixture was filtered, and the solvent was removed in vacuo. The crude product was chromatographed on 50 g of silica. The column was eluted with MeOH-EtOAc (1:9) to give 70 mg of
 10 the desired product (67%) as a yellow solid: mp 68 °C (decomp.); Anal. Calcd for $C_{38}H_{43}N_6O_3F_1 + 1.0H_2O$: C, 68.24; H, 6.78; N, 12.57. Found: C, 68.43; H, 6.60; N, 12.46.

5-Acetyl-2-((2-aminoethyl)oxy)methyl-4-(4-fluoro)phenyl
 15 -1,4-dihydro-6-methyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (242): To a solution of 5 - a c e t y l - 2 - ((2 - a z i d o e t h -
 y l) o x y) m e t h y l - 4 - (4 - f l u o r o) p h e n y l - 1 , 4 - d i h y d r o - 6 - m e t h -
 y 1 - 3 - (N - (3 -
 20 (4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (48 mg, 0.074 mmol) in 3 mL of EtOAc at 0 °C was added 1 M (Me)₃P in THF (0.19 mL, 0.19 mmol), and water (13 mL, 0.74 mmol). The reaction mixture was stirred at room temperature for 4 hours, and the solvent was removed in
 25 vacuo. The crude product was chromatographed on 100 g of silica packed with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:10). The column was eluted with NH₃ (2N in MeOH)-MeOH-CHCl₃ (1:2:10) to give 38 mg (82%) of the desired product as a yellow solid: mp 75 °C (decomp.); Anal. Calcd for
 30 $C_{38}H_{45}N_6O_3F_1 + 1.1CH_2Cl_2$: C, 65.39; H, 6.62; N, 7.80. Found: C, 65.01; H, 6.82; N, 7.85.

EXAMPLE 243

35 5-Carboxamido-3-(N-(3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-2-((2,2,2-trifluoroethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phen-

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ylpyridine (243): A mixture of 5-carboxamido-2-((2,2,2-trifluoroethyl)oxy)methyl-1,4-dihydro-6-methyl-4-(4-nitro)phenylpyridine-3-carboxylic acid (45 mg, 0.109 mmol), DCC (45 mg, 0.218 mmol), and DMAP (11 mg, 0.087 mmol) in 10 mL of dry dichloromethane were stirred at room temperature for 45 minutes. 1-(3-Amino)propyl-4-ethoxycarbonyl-4-phenylpiperidine (41 mg, 0.140 mmol) was added to the reaction mixture and stirred at room temperature for 17 hours. The reaction mixture was filtered, the solvent was removed in vacuo, and the crude product was chromatographed on 200 g of silica packed with MeOH-EtOAc (1:4). The column was eluted with the same solvent to give 26 mg (47%) of the title compound as a yellow solid: mp 91 °C (decomp.); Anal. Calcd for $C_{34}H_{40}N_5F_3O_7 + 0.3CHCl_3$: C, 56.96; H, 5.61; N, 9.68. Found: C, 56.94; H, 5.73; N, 9.61.

EXAMPLE 244

5-Acetyl-2-((2-aminoethyl)oxy)methyl-3-(N-(3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-1,4-dihydro-6-methyl-4-(3,4-methylenedioxy)phenylpyridine (244)
5-Acetyl-2-((2-azidoethyl)oxy)methyl-3-(N-(3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(3,4-methylenedioxy)phenyl-1,4-dihydro-6-methylpyridine: A solution of 5-acetyl-2-((2-azidoethyl)oxy)methyl-4-(3,4-methylenedioxy)phenyl-1,4-dihydro-6-methylpyridine-3-carboxylic acid (60 mg, 0.150 mmol), DCC (62 mg, 0.300 mmol), and DMAP (15 mg, 0.120 mmol) in 3 mL of dry dichloromethane were stirred at room temperature for 2 hours. The reaction mixture was charged with 1-(3-amino)propyl-4-ethoxycarbonyl-4-phenylpiperidine (57 mg, 0.195 mmol) and the reaction mixture was stirred at room temperature for 16 hours. The reaction mixture was filtered, and the solvent was removed in vacuo. The

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crude product was chromatographed on 180 g of silica packed with MeOH-EtOAc (1:9). The column was eluted with the same solvent to give 62 mg (62%) of the title compound as a yellow solid: mp 55 °C (decomp.); Anal.

5 Calcd for $C_{36}H_{44}N_6F_3O_7 + 1.0H_2O + 0.5EtOAc$: C, 62.11; H, 6.86; N, 11.44. Found: C, 62.06; H, 6.48; N, 11.45.

5-Acetyl-2-((2-aminoethyl)oxy)methyl-3-(N-(3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-1,4-dihydro-6-methyl-4-(3,4-methylenedioxy)phenylpyridine (244): To a solution of 5-acetyl-2-((2-azidoethyl)oxy)methyl-3-(N-(3-(4-ethoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-4-(3,4-methylenedioxy)phenyl-1,4-dihydro-6-methylpyridine (45 mg, 0.067 mmol) in 3 mL of EtOAc at 0 °C was added 1 M $(Me)_3P$ in THF (0.17 mL, 0.167 mmol), and water (12 mL, 0.67 mmol). The reaction mixture was stirred at room temperature for 3.5 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with NH_3 (2N in MeOH)-MeOH- $CHCl_3$ (1:2:10). The column was eluted with NH_3 (2N in MeOH)-MeOH- $CHCl_3$ (1:2:10) to give 31 mg (72%) of the desired product as a yellow solid: mp 55 °C (decomp.); Anal. Calcd for $C_{36}H_{46}N_6O_7 + 1.0H_2O + 0.3CHCl_3$: C, 62.23; H, 6.95; N, 8.00. Found: C, 62.14; H, 6.85; N, 7.78.

EXAMPLE 245

30 5-Acetyl-2-((2-aminoethyl)oxy)methyl-4-(4-fluoro)phenyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-6-methylpyridine (245)

35 5-Acetyl-2-((2-azidoethyl)oxy)methyl-4-(4-fluoro)phenyl-1,4-dihydro-3-(N-(3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl))carboxamido-6-methylpyridine: A solution

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of 5-acetyl-2-((2-azidoethyl)oxy)methyl-4-(4-fluoro)phenyl-1,4-dihydro-6-methylpyridine-3-carboxylic acid (50 mg, 0.134 mmol), DCC (55 mg, 0.268 mmol), and DMAP (13 mg, 0.107 mmol) in 4 mL of dry dichloromethane were stirred at room temperature for 2 hours followed by addition of 1-(3-amino)propyl-4-methoxycarbonyl-4-phenylpiperidine (48 mg, 0.174 mmol). The resulting mixture was stirred at room temperature for 2 days. The reaction mixture was filtered, and the solvent was removed in vacuo. The crude product was chromatographed on 200 g of silica. The column was eluted with MeOH-EtOAc (1:9) to give 68 mg of the desired product (80%) as a yellow solid: mp 48 °C (decomp.); Anal. Calcd for $C_{38}H_{43}N_6O_3F_1 + 0.3CHCl_3$: C, 61.62; H, 6.23; N, 12.57. Found: C, 61.75; H, 6.47; N, 12.53.

5-Acetyl-2-((2-aminoethyl)oxy)methyl-4-(4-fluoro)phenyl-1,4-dihydro-3-(N-3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl)carboxamido-6-methylpyridine (245): To a solution of 5-acetyl-2-((2-azidoethyl)oxy)methyl-4-(4-fluoro)phenyl-1,4-dihydro-3-(N-3-(4-methoxycarbonyl-4-phenylpiperidin-1-yl)propyl)carboxamido-6-methylpyridine (52 mg, 0.0823 mmol) in 3 mL of EtOAc at 0 °C was added 1 M $(Me)_3P$ in THF (0.21 mL, 0.206 mmol), and water (15 mL, 0.823 mmol). The reaction mixture was stirred at room temperature for 3.5 hours, and the solvent was removed in vacuo. The crude product was chromatographed on 100 g of silica packed with NH_3 (2N in MeOH)-MeOH- $CHCl_3$ (1:2:20). The column was eluted with NH_3 (2N in MeOH)-MeOH- $CHCl_3$ (1:2:20) to give 40 mg (85%) of the desired product as a yellow solid: mp 54 °C (decomp.); Anal. Calcd for $C_{31}H_{43}N_6O_5F_1 + 0.8EtOAc + 0.8CHCl_3$: C, 57.06; H, 6.87; N, 7.61. Found: C, 57.36; H, 6.30; N, 7.40.

EXAMPLE 246

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6-Ethyl-1,4-dihydro-5-(2-hydroxyethoxycarbonyl)-2-(methyloxy)methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (246): A solution of 50 mg of 6-ethyl-1,4-dihydro-2-(methyloxy)methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-carboxylic acid (0.078 mmol), 30 mg of DMAPECD (0.157 mmol), and DMAP (19 mg, 0.157 mmol) in 3 mL of dry dichloromethane were stirred at room temperature for 2 hours before addition of ethyleneglycol (24 mg, 0.39 mmol). The reaction mixture was heated at reflux temperature for 17 hours. The reaction mixture was cooled, washed sequentially with saturated NH_4Cl solution (2 X 5 mL), aqueous 0.1 N HCl solution (3 X 5 mL), brine (5 mL), dried (Na_2SO_4), and the solvent was removed under reduced pressure. The crude product was chromatographed on 220 g of silica packed with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:50). The column was eluted with NH_3 (2N in MeOH)-MeOH- CHCl_3 (0.5 L of 1:2:30) to give 38 mg (75%) of the desired product as a yellow solid: mp 73 °C(decomp.); Anal. Calcd for $\text{C}_{39}\text{H}_{46}\text{N}_4\text{O}_7 + 0.5 \text{H}_2\text{O}$: C, 67.71; H, 6.85; N, 8.10. Found: C, 67.64; H, 6.96; N, 7.81.

EXAMPLE 247

6-Ethyl-1,4-dihydro-5-N-((2-methoxy)ethyl)carboxamido-2-(methyloxy)methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (247): A solution of 50 mg of 6-ethyl-1,4-dihydro-2-(methyloxy)methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-carboxylic acid (0.078 mmol), 30.1 mg of DMAPECD (0.157 mmol), DMAP (19.2 mg, 0.157 mmol), and 2-aminoethylmethylether (29 mg, 0.390 mmol) in 3 mL of dry dichloromethane were heated at reflux temperature for 20 hours. The reaction mixture was cooled, washed sequentially with aqueous 0.1 N HCl solution (3 X 5 mL),

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brine (5 mL), dried (Na_2SO_4), and the solvent was removed under reduced pressure. The crude product was chromatographed on 220 g of silica packed with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:50). The column was eluted with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:50) to give 38 mg (70%) of the desired product as a yellow solid: mp 70 °C (decomp.); Anal. Calcd for $\text{C}_{40}\text{H}_{49}\text{N}_5\text{O}_6$: C, 69.03; H, 7.11; N, 10.06. Found: C, 69.00; H, 7.27; N, 9.97.

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EXAMPLE 248

6-Ethyl-1,4-dihydro-2-((methyloxy)methyl-5-N-(morpholin-4-yl)carboxamido-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine (248): A solution of 60 mg of 6-ethyl-1,4-dihydro-2-(methyloxy)methyl-4-(4-nitro)phenyl-3-(N-(3-(4,4-diphenylpiperidin-1-yl)propyl))carboxamidopyridine-5-carboxylic acid ((0.094 mmol), 36 mg of DMAPECD (0.188 mmol), 29 mg of DMAP (0.235 mmol), and 14.4 mg of 4-aminomorpholine (0.141 mmol) in 3 mL of dry dichloromethane were heated at reflux temperature for 15 hours. The reaction mixture was cooled to room temperature, sequentially washed with aqueous 0.1 N HCl solution (4 X 3 mL), brine (mL), dried (Na_2CO_3), and the solvent was removed in vacuo. The residue was chromatographed on 50 g of silica packed with NH_3 (2N in MeOH)-MeOH- CHCl_3 (1:2:50). The column was eluted with NH_3 (2N in MeOH)-MeOH- CHCl_3 (0.5 L of 1:2:50 and 1 L of 1:2:40) to give 34 mg (50%) of the desired product as a yellow solid: mp 112 °C (decomp.); Anal. Calcd for $\text{C}_{41}\text{H}_{50}\text{N}_6\text{O}_6 + 1.0\text{H}_2\text{O}$: C, 66.47; H, 7.07; N, 11.34. Found: C, 66.29; H, 6.94; N, 11.26.

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EXAMPLE 249

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(3-nitrophenyl)-5-(N-(3-(4,4-diphenylpiperidin-1-

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yl)propyl)carboxamido)-pyridine (249). A solution of acetoacetic acid *N*-(3-(4,4-diphenylpiperidin-1-yl)propyl)amide (200 mg, 0.528 mmol), methyl 3-aminocrotonate (62.7 mg, 0.528 mmol), and 3-nitrobenzaldehyde (79.8 mg, 0.528 mmol) in 2-propanol (5 ml) was refluxed for 96 hours. Then the solvent was removed, and the residue was flash chromatographed (Hexane : EtOAc : Et₃N = 50 : 50 : 3; Hexane : EtOAc : Et₃N = 10 : 90 : 6; and EtOAc : Et₃N = 10 : 1) to give a yellow solid. It was recrystallized from EtOAc/Hexane to afford yellow crystals (96 mg, 30%): mp 192-193 °C. Anal. Calcd for C₃₆H₄₀N₄O₅: C, 70.00, H, 6.69, N, 9.06. Found. C, 70.24, H, 6.31, N, 8.84.

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EXAMPLE 250

1,4-Dihydro-3-methoxycarbonyl-2,6-dimethyl-4-(3,4-methylenedioxyphenyl)-5-(*N*-(3-(4-phenylpiperidin-1-yl)propyl)carboxamido)-pyridine (250). *N*-(3-(4-Phenylpiperidin-1-yl)propyl) acetoacetamide (200 mg, 0.66 mmol) was mixed with methyl 3-aminocrotonate (76 mg, 0.66 mmol) and piperonal (99 mg, 0.66 mmol) in 1-butanol (5 ml). The mixture was heated at reflux temperature for 4 days and then concentrated to give a brown oil. It was dissolved in chloroform and flash chromatographed over silica gel (15 g) eluting with EtOAc/Et₃N (20:1) to afford a yellow oil (54 mg, 15% yield). Recrystallization from EtOAc/Hexane gave yellow crystals (19 mg): mp 161-165 °C. Anal. Calcd for C₃₁H₃₇N₃O₅: C, 70.03; H, 7.01; N, 7.90. Found: C, 69.87; H, 7.07; N, 7.62.

EXAMPLE 251

5-Carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)-3-{*N*-[3-(piperidin-1-yl)propyl]}carboxamidopyridine (251). To a mixture of 5-carboxamido-1,4-dihydro-2,6-dimethyl-4-(4-nitrophenyl)pyridine-3-carboxylic acid (212

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mg, 0.668 mmol, 1.00 equiv), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (195 mg, 1.02 mmol, 1.52 equiv) and 4-dimethylaminopyridine (91 mg, 0.74 mmol, 1.1 equiv) in anhydrous CH_2Cl_2 (3 mL) was added a solution of
5 1-(3-amino)propylpiperidine (115.9 mg, 0.815 mmol, 1.22 equiv, Bates, R. J.; Cymerman-Craig, J.; Moyie, M.; Yong, T. J. *J. Chem. Soc.* 1956, 388) in CH_2Cl_2 (3.7 mL), and the mixture was stirred at room temperature under argon for 20 hours. Aqueous NaOH (1 M, 50 mL) was added and the
10 mixture was extracted with CH_2Cl_2 -isopropanol (3:1, 3 x 50 mL). The combined organic solutions were dried over Na_2SO_4 and concentrated to give 635.7 mg of dark brown oil. This oil was purified by flash chromatography (SiO_2 , Cl_3CCH_3 -MeOH-methanolic ammonia (2 M) 70:15:15) to afford
15 385 mg of a yellow oil. This yellow oil was further purified by HPLC with a 25 x 300 mm Waters NovaPak 6 μm SiO_2 radial compression column and UV detection at 252 nm. The column was eluted with the following gradient at 25 mL/min: initial conditions CH_2Cl_2 :(CH_2Cl_2 -MeOH- Et_2NH
20 93.8:6:0.2) 50:50, duration 30 minutes, ramped to 13:87 over 30 minutes. The pure product was obtained as a yellow solid, 167.4 mg (56%): mp 170 °C; Anal. Calcd for $\text{C}_{23}\text{H}_{31}\text{N}_5\text{O}_4 \cdot 0.1 \text{ CH}_2\text{Cl}_2$: C, 61.65; H, 6.99; N, 15.56. Found: C, 61.61; H, 7.16; N, 15.62.

25

Binding affinities were measured for selected compounds of the invention at six cloned human alpha-1 and alpha-2 receptor subtypes, as well as at the L-type calcium channel. The protocols for these experiments are given
30 below. Table 1 shows the results.

Protocol for the Determination of the Potency of α_1 Antagonists

The activity of compounds at the different human
35 receptors was determined in vitro using cultured cell lines that selectively express the receptor of interest. These cell lines were prepared by transfecting the cloned

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cDNA or cloned genomic DNA or constructs containing both genomic DNA and cDNA encoding the human α -adrenergic receptors as follows:

5 **α_{1A} Human Adrenergic Receptor:** The entire coding region of α_{1A} (1719 bp), including 150 basepairs of 5' untranslated sequence (5' UT) and 300 bp of 3' untranslated sequence (3' UT), was cloned into the BamHI and ClaI sites of the polylinker-modified eukaryotic
10 expression vector pCEXV-3, called EXJ.HR. The construct involved the ligation of partial overlapping human lymphocyte genomic and hippocampal cDNA clones: 5' sequence were contained on a 1.2 kb SmaI-XhoI genomic fragment (the vector-derived BamHI site was used for
15 subcloning instead of the internal insert-derived SmaI site) and 3' sequences were contained on an 1.3 kb XhoI-ClaI cDNA fragment (the ClaI site was from the vector polylinker). Stable cell lines were obtained by cotransfection with the plasmid α_{1A} /EXJ (expression
20 vector containing the α_{1A} receptor gene) and the plasmid pGCcos3neo (plasmid containing the aminoglycoside transferase gene) into LM(tk⁻), CHO, and NIH3T3 cells, using calcium phosphate technique. The cells were grown, in a controlled environment (37°C., 5% CO₂), as monolayers
25 in Dulbecco's modified Eagle's Medium (GIBCO, Grand Island, NY) containing 25mM glucose and supplemented with 10% bovine calf serum, 100 units/ml penicillin g, and 100 μ g/ml streptomycin sulfate. Stable clones were then selected for resistance to the antibiotic G-418 (1
30 mg/ml), and membranes were harvested and assayed for their ability to bind [³H]prazosin as described below (see "Radioligand Binding assays").

α_{1B} Human Adrenergic Receptor: The entire coding region
35 of α_{1B} (1563 bp), including 200 basepairs and 5' untranslated sequence (5' UT) and 600 bp of 3' untranslated sequence (3' UT), was cloned into the EcoRI

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site of pCEXV-3 eukaryotic expression vector. The construct involved ligating the full-length containing EcoRI brainstem cDNA fragment from λ ZapII into the expression vector. Stable cell lines were selected as described above.

α_{1c} Human Adrenergic Receptor: The entire coding region of α_{1c} (1401 bp), including 400 basepairs of 5' untranslated sequence (5' UT) and 200 bp of 3' untranslated sequence (3' UT), was cloned into the KpnI site of the polylinker-modified pCEXV-3-derived eukaryotic expression vector, EXJ.RH. The construct involved ligating three partial overlapping fragments: a 5' 0.6kb HincII genomic clone, a central 1.8 EcoRI hippocampal cDNA clone, and a 3' 0.6Kb PstI genomic clone. The hippocampal cDNA fragment overlaps with the 5' and 3' genomic clones so that the HincII and PstI sites at the 5' and 3' ends of the cDNA clone, respectively, were utilized for ligation. This full-length clone was cloned into the KpnI site of the expression vector, using the 5' and 3' KpnI sites of the fragment, derived from vector (i.e., pBluescript) and 3'-untranslated sequences, respectively. Stable cell lines were selected as described above.

Radioligand Binding Assays: Transfected cells from culture flasks were scraped into 5ml of 5mM Tris-HCl, 5mM EDTA, pH 7.5, and lysed by sonication. The cell lysates were centrifuged at 1000 rpm for 5 min at 4°C, and the supernatant was centrifuged at 30,000 x g for 20 min at 4°C. The pellet was suspended in 50mM Tris-HCl, 1mM MgCl₂, and 0.1% ascorbic acid at pH 7.5. Binding of the α_1 antagonist [³H]prazosin (0.5 nM, specific activity 76.2 Ci/mmol) to membrane preparations of LM(tk-) cells was done in a final volume of 0.25 ml and incubated at 37°C for 20 min. Nonspecific binding was determined in the presence of 10 μ M phentolamine. The reaction was stopped

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by filtration through GF/B filters using a cell harvester. Inhibition experiments, routinely consisting of 7 concentrations of the tested compounds, were analyzed using a non-linear regression curve-fitting
5 computer program to obtain K_i values.

α_2 Human Adrenergic Receptors: To determine the potency of α_1 antagonists at the α_2 receptors, LM(tk-) cell lines stably transfected with the genes encoding the α_{2A} , α_{2B} ,
10 and α_{2C} receptors were used. The cell line expressing the α_{2A} receptor is designated L- α_{2A} , and was deposited on November 6, 1992 under ATCC Accession No. CRL 11180. The cell line expressing the α_{2B} receptor is designated L-NGC- α_{2B} , and was deposited on October 25, 1989 under ATCC
15 Accession No. CRL10275. The cell line expressing the α_{2C} receptor is designated L- α_{2C} , and was deposited on November 6, 1992 under ATCC Accession No. CRL-11181. Cell lysates were prepared as described above (see Radioligand Binding Assays), and suspended in 25mM
20 glycylglycine buffer (pH 7.6 at room temperature). Equilibrium competition binding assay were performed using [3H]rauwolscine (0.5nM), and nonspecific binding was determined by incubation with 10 μ M phentolamine. The bound radioligand was separated by filtration through
25 GF/B filters using a cell harvester.

Determination of the Activity of α_1 Antagonists at Calcium Channels

The potency of α_1 antagonists at calcium channels was
30 determined in competition binding assays of [3H]nitrendipine to membrane fragments of rat cardiac muscle, essentially as described by Glossman and Ferry (Methods in Enzymology 109:513-550, 1985). Briefly, the tissue was minced and homogenized in 50mM Tris-HCl (pH
35 7.4) containing 0.1mM phenylmethylsulfonyl fluoride. The homogenates were centrifuged at 1000 g for 15 minutes, the resulting supernatant was centrifuged at 45,000 g for

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15 minutes. The 45,000 g pellet was suspended in buffer and centrifuged a second time. Aliquots of membrane protein were incubated for 30 minutes at 37°C in the presence of [3H]nitrendipine (1nM), and nonspecific
5 binding was determined in the presence of 10μM nifedipine. The bound radioligand was separated by filtration through GF/B filters using a cell harvester.

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
1	pKi	5.59	6.39	7.52	5.62	5.48	6.77	5.18
	SEM	0.10	0.15	0.23	0.15	0.21	0.14	0.39
	n	3	3	3	3	3	3	2
(\pm)-2	pKi	6.22	6.48	8.73	6.44	6.38	6.49	3.7
	SEM	0.04	0.08	0.08	0.03	0.01	0.02	0.41
	n	4	4	4	3	3	3	2
(+) -2	pKi	6.40	6.35	7.69	6.52	6.40	6.53	4.11
	SEM	0.19	0.06	0.13	0.18	0.18	0.06	
	n	3	3	2	2	2	2	2
(-)-2	pKi	6.46	6.39	8.91	6.83	6.56	6.78	2.74
	SEM	0.16	0.04	0.07	0.06	0.05	0.04	
	n	3	3	3	2	2	2	1
3	pKi	6.84	7.19	8.23	6.99	7.65	7.29	3.00
	SEM	0.02	0.01	0.04	0.25	0.02	0.11	
	n	3	3	3	3	3	3	1
4	pKi	6.71	6.89	7.17	6.26	5.99	6.30	6.01
	SEM	0.03	0.06	0.07	0.04	0.03	0.06	
	n	3	3	3	4	4	4	1
5	pKi	5.74	6.08	7.95	5.65	5.67	4.61	5.34
	SEM	0.13	0.12	0.19	0.03	0.17	0.17	0.03
	n	4	4	4	2	2	2	3

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
6	pK _i	5.95	6.69	6.83	6.08	6.35	6.62	5.80
	SEM	0.15	0.21	0.27	0.13	0.14	0.17	0.10
	n	3	3	3	3	3	3	2
7	pK _i	5.93	6.54	6.21	5.42	5.79	5.91	6.06
	SEM	0.05	0.04	0.02				
	n	3	3	3	1	1	1	1
8	pK _i	6.42	6.73	7.12	6.08	5.73	6.47	4.94
	SEM	0.05	0.09	0.03	0.08	0.01	0.05	
	n	3	3	3	2	2	2	1
9	pK _i	5.77	6.47	7.62	5.66	6.26	5.88	4.72
	SEM	0.03	0.29	0.15	0.04	0.09	0.02	0.13
	n	3	3	3	4	3	3	3
10	pK _i	6.35	6.91	8.75	5.63	5.48	5.91	5.12
	SEM	0.10	0.04	0.01	0.09	0.11	0.12	0.07
	n	3	3	3	3	3	3	2
11	pK _i	6.52	6.64	8.95	5.95	6.06	6.24	5.64
	SEM	0.12	0.14	0.12	0.03	0.02	0.02	0.02
	n	3	3	3	3	3	3	2
12	pK _i	6.42	6.82	8.74	6.11	5.90	6.06	5.42
	SEM	0.03	0.02	0.01	0.08		0.04	0.10
	n	3	3	2	2	2	2	3

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
13	pKI	6.41	6.78	8.14	5.90	5.76	6.19	5.05
	SEM	0.08	0.06	0.15	0.03	0.05	0.04	0.06
	n	3	3	3	2	2	2	2
14	pKI	5.39	5.58	7.39	5.54	5.87	5.96	
	SEM	0.28	0.30	0.21	0.05	0.02	0.06	
	n	2	2	2	2	2	2	
15	pKI	6.38	6.78	8.2	5.61	5.47	5.95	5.14
	SEM	0.02	0.04	0.05	0.03	0.04	0.05	
	n	3	3	3	2	2	2	1
16	pKI	6.37	6.76	8.23	5.95	5.74	6.42	6.09
	SEM	0.01	0.03	0.07	0.04	0.15	0.04	
	n	3	3	3	2	2	2	1
17	pKI	6.90	7.38	9.27	6.46	6.85	7.57	5.00
	SEM	0.04	0.10	0.23	0.06	0.05	0.02	
	n	3	3	3	2	2	2	1
18	pKI	6.05	6.76	7.16	5.67	5.79	6.03	6.79
	SEM	0.06	0.10	0.09	0.03	0.05	0.05	0.15
	n	3	3	3	3	3	3	2
19	pKI	6.50	6.57	8.87	5.89	6.04	6.38	5.13
	SEM	0.04	0.02	0.21				0.05
	n	3	3	3	1	1	1	2

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		alpha-1			alpha-2			Ca
		1a	1b	1c	2a	2b	2c	
20	pKi	5.87	6.92	8.42	5.75	5.88	6.09	5.94
	SEM	0.12	0.67	0.06	0.06	0.03	0.02	0.15
	n	3	3	3	2	2	2	3
21	pKi	6.31	6.69	8.15	5.68	5.97	6.11	6.00
	SEM	0.04	0.07	0.05	0.00	0.03	0.02	0.19
	n	3	3	3	2	2	2	2
22	pKi	6.13	6.86	7.44	5.80	6.04	6.20	6.43
	SEM	0.06	0.06	0.03	0.08	0.22	0.00	0.14
	n	3	3	3	3	3	3	2
23	pKi	6.19	6.67	7.84	6.02	6.25	6.33	6.54
	SEM	0.06	0.04	0.07	0.06	0.03	0.02	0.02
	n	3	3	3	3	3	3	2
24	pKi	6.49	6.94	8.73	6.04	5.90	6.8	5.71
	SEM	0.03	0.04	0.06	0.03	0.01	0.34	0.09
	n	3	3	3	2	2	2	3
25	pKi	6.19	6.48	7.47	5.82	6.30	5.99	5.94
	SEM	0.09	0.02	0.08	0.01	0.33	0.00	0.16
	n	3	3	3	2	2	2	2
26	pKi	6.28	6.36	8.15	5.67	6.01	5.83	7.06
	SEM	0.03	0.03	0.21	0.08	0.05	0.06	
	n	2	3	3	2	2	2	1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
27	pKi	6.42	6.49	8.44	5.71	5.98	5.92	6.23
	SEM	0.04	0.04	0.16	0.05	0.06	0.02	
	n	3	3	3	2	2	2	1
28	pKi	6.36	6.62	8.02	5.64	5.78	6.20	4.76
	SEM	0.06	0.08	0.10	0.22	0.09	0.00	
	n	3	3	3	2	2	2	1
29	pKi	6.58	6.85	8.83	6.16	6.20	6.40	4.86
	SEM	0.05	0.07	0.08	0.08	0.10	0.07	
	n	3	3	3	2	2	2	1
30	pKi	6.81	7.27	8.52	6.93	6.63	7.31	7.02
	SEM	0.01	0.08	0.41	0.05	0.10	0.12	0.09
	n	3	3	2	3	3	3	2
31	pKi	6.95	7.69	8.93	6.80	6.86	7.28	
	SEM	0.06	0.01	0.12	0.08	0.10	0.11	
	n	3	3	3	2	2	2	
32	pKi	6.13	6.52	7.88				5.80
	SEM	0.01	0.05	0.07				0.04
	n	2	2	2				2
37	pKi	6.16	6.70	7.64	6.15	5.97	6.24	5.87
	SEM				0.10	0.00	0.00	
	n	1	1	1	2	2	2	1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		alpha-1			alpha-2			Ca
		1a	1b	1c	2a	2b	2c	
38	pKI	6.21	6.38	8.50	6.40	6.04	6.49	5.15
	SEM	0.08	0.03	0.09	0.07	0.02	0.02	0.11
	n	3	3	3	4	4	4	2
39	pKI	5.77	5.93	7.23	6.02	5.74	6.09	4.35
	SEM	0.06	0.05	0.01	0.03	0.02	0.03	0.12
	n	3	3	3	3	3	3	3
40	pKI	6.26	6.56	7.86	5.73	5.75	6.01	4.8
	SEM	0.05	0.06	0.01	0.06	0.07	0.02	0.11
	n	2	2	2	3	3	3	2
41	pKI	6.30	6.53	8.74	6.37	6.22	6.36	
	SEM	0.07	0.08	0.03				
	n	2	2	2	1	1	1	
42	pKI	6.35	6.55	8.90	6.49	6.64	6.77	
	SEM	0.08	0.02	0.03				
	n	2	2	2	1	1	1	
43	pKI	6.50	6.74	8.62	6.18	6.36	6.40	4.73
	SEM	0.06	0.06	0.21	0.02	0.00	0.07	
	n	3	3	3	2	2	2	1
44	pKI	5.23	5.08	5.77				4.78
	SEM	0.09	0.16	0.08				0.04
	n	2	2	3				2

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
(±)-45	pK _i	7.18	7.87	9.63	6.55	6.67	7.09	5.13
	SEM	0.03	0.05	0.11	0.02	0.04	0.05	0.03
	n	3	3	3	3	3	3	4
(-)-45	pK _i	7.39	8.04	9.74	6.47	6.64	7.86	5.36
	SEM	0.13	0.05	0.07				
	n	3	3	3	1	1	1	1
(+) -45	pK _i	6.75	7.24	8.03	6.62	7.04	7.65	
	SEM	0.21	0.00	0.08				
	n	3	2	3	1	1	1	
46	pK _i	6.30	6.62	7.69	6.17	6.31	6.61	5.13
	SEM	0.06	0.04	0.12	0.02	0.01	0.02	0.19
	n	4	4	4	3	3	3	2
47	pK _i	6.29	6.58	8.93	6.22	6.36	6.43	4.75
	SEM	0.08	0.03	0.16	0.02	0.02	0.03	
	n	3	3	3	3	3	3	1
48	pK _i	8.01	8.58	9.28	7.76	6.09	6.38	6.32
	SEM	0.03	0.10	0.07				
	n	3	3	3	1	1	1	1
49	pK _i	6.94	6.72	8.56	6.63	6.42	6.86	5.37
	SEM	0.07	0.27	0.16	0.03	0.02	0.05	
	n	3	3	2	2	2	2	1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
50	pKi	5.71	5.52	7.07	5.82	5.56	6.18	5.02
	SEM	0.07	0.04	0.17	0.27	0.21	0.28	
	n	3	3	3	2	2	2	
51	pKi	5.01	5.30	6.32	6.35	6.29	6.60	3
	SEM	0.05	0.22	0.07	0.05	0.14	0.01	
	n	3	3	2	2	2	2	
52	pKi	5.94	7.11	8.06	6.29	6.10	6.58	5.29
	SEM	0.49	0.06	0.11				
	n	2	2	2	1	1	1	
53	pKi	6.49	6.87	7.83	6.18	6.34	6.67	5.54
	SEM	0.03	0.16	0.21				
	n	3	3	3	1	1	1	
54	pKi	6.46	6.76	7.91	6.33	6.52	6.80	4.23
	SEM	0.03	0.11	0.11	0.02	0.14	0.06	
	n	3	3	3	2	2	2	
55	pKi	6.17	6.45	7.99	6.21	6.51	6.78	3
	SEM	0.06	0.05	0.10	0.02	0.16	0.04	
	n	3	3	3	2	2	2	
56	pKi	6.20	6.66	8.52	6.57	6.89	6.73	5.19
	SEM	0.03	0.04	0.01	0.01		0.03	
	n	2	2	2	2	2	2	

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
57	pK _i	5.79	5.91	6.22	6.71	5.73	6.80	3.00
	SEM	0.02	0.01	0.03	0.06	0.03	0.09	
	n	3	3	3	3	3	3	
58	pK _i	5.52	5.64	6.48	8.08	5.84	7.30	3.78
	SEM	0.02	0.01	0.12	0.02	0.02	0.09	
	n	3	3	3	3	3	3	
59	pK _i	6.29	6.41	6.61				
	SEM	0.01	0.02	0.03				
	n	2	2	2				
60	pK _i	6.70	7.11	8.56	8.26	7.16	7.17	3.80
	SEM	0.02	0.04	0.11	0.03	0.03	0.01	
	n	2	3	3	3	3	3	
61	pK _i	6.07	6.37	8.42	6.12	6.22	6.32	4.99
	SEM	0.01	0.04	0.07	0.07	0.10	0.03	
	n	3	3	3	3	3	3	
62	pK _i	6.47	6.50	8.58	7.61	7.24	7.31	4.71
	SEM	0.01	0.03	0.17	0.11	0.02	0.04	
	n	3	3	3	3	3	3	
63	pK _i	7.35	7.73	7.41	6.02	6.88	6.77	4.18
	SEM	0.02	0.06	0.04	0.05	0.10	0.01	
	n	3	3	3	2	2	2	

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		alpha-1			alpha-2			Ca
		1a	1b	1c	2a	2b	2c	
64	pKi	6.31	6.45	7.45	6.16	6.36	6.32	4.01
	SEM	0.10	0.05	0.02				0.00
	n	2	2	2	1	1	1	2
65	pKi	6.89	7.24	8.98	6.70	7.01	7.08	5.51
	SEM	0.02	0.06	0.04	0.08	0.01	0.02	
	n	3	3	3	2	2	2	1
66	pKi	5.45	5.36	6.59	5.53	5.35	6.24	6.22
	SEM	0.09	0.07	0.04	0.02	0.01	0.02	
	n	2	2	2	2	2	2	1
67	pKi	5.96	6.18	6.48	6.45	5.79	7.00	
	SEM	0.03	0.15	0.1	0.02	0.01	0.02	
	n	4	4	4	3	3	3	
73	pKi	6.69	6.83	9.18	6.10	6.17	6.56	6.12
	SEM	0.03	0.05	0.05	0.09	0.01	0.03	
	n	2	2	3	2	2	2	1
74	pKi	7.23	7.72	9.30	7.23	7.05	7.63	5.28
	SEM	0.05	0.04	0.03	0.03	0.05	0.05	
	n	3	3	3	2	2	2	1
75	pKi	5.36	5.41	6.10	5.54	5.51	5.91	5.45
	SEM	0.05	0.28		0.01	0.01	0.04	
	n	3	3	1	2	2	2	1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		alpha-1			alpha-2			Ca
		1a	1b	1c	2a	2b	2c	
76	pKI	5.89	5.88	6.63	6.96	5.64	7.70	5.49
	SEM	0.10	0.06	0.11	0.05	0.15	0.24	0
	n	4	4	4	2	2	2	2
77	pKI	6.83	7.16	8.30	6.95	7.08	7.42	5.94
	SEM	0.03	0.06	0.13	0.04	0.02	0.08	0.04
	n	3	3	3	3	3	3	2
78	pKI	6.75	6.96	8.37	6.14	6.26	6.82	5.5
	SEM	0.05	0.02	0.13	0.10	0.13	0.03	0.03
	n	3	3	3	3	3	3	2
79	pKI	6.99	7.33	7.76	6.84	7.28	7.21	6.17
	SEM	0.01	0.03	0.09	0.13	0.08	0.12	
	n	3	3	3	4	4	4	1
81	pKI	6.39	6.62	8.72	6.75	6.79	6.91	4.49
	SEM	0.02	0.02	0.10				0.25
	n	3	2	3	1	1	1	2
89	pKI	6.46	6.85	6.30	5.63	5.71	6.30	6.09
	SEM	0.08	0.06	0.04	0.10	0.04	0.04	0.18
	n	3	3	3	3	3	3	3
90	pKI	6.52	6.87	7.56	6.13	6.04	6.79	6.63
	SEM	0.07	0.03	0.04	0.03		0.35	0.10
	n	3	3	3	2	2	2	3

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
91	pK _i	6.29	6.54	8.04	6.06	6.00	6.31	6.55
	SEM	0.25	0.27	0.05	0.05	0.05	0.05	
	n	3	3	3	3	3	3	1
92	pK _i	6.68	7.23	8.51	5.50	6.14	6.12	5.38
	SEM	0.07	0.11	0.17				0.25
	n	3	3	3	1	1	1	2
(±)-93	pK _i	5.98	6.57	8.87	5.48	5.93	5.88	6.1
	SEM	0.07	0.12	0.08	0.07	0.04	0.04	0.01
	n	3	3	3	2	2	2	2
(+) -93	pK _i	5.98	6.73	7.52	6.04	6.01	6.36	6.72
	SEM	0.5	0.08		0.11	0.06	0.01	
	n	2	2	1	2	2	2	1
(-)-93	pK _i	6.56	6.95	8.92	6.13	6.01	6.27	5.89
	SEM			0.25	0.09	0.09	0.02	
	n	1	1	2	2	2	2	1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		alpha-1			alpha-2			Ca
		1a	1b	1c	2a	2b	2c	
95	pKi	5.33	5.72	8.11	6.23	5.55	5.61	3.64
	SEM	0.06	0.09	0.01	0.08	0.01	0.03	0.30
	n	3	3	3	3	3	3	3
96	pKi	5.42	5.28	7.57	5.64	5.93	6.04	3
	SEM	0.03	0.06	0.08	0.03	0.02	0.05	
	n	3	3	3	3	3	3	2
(±)-97	pKi	5.56	5.99	8.54	5.55	5.93	5.61	3
	SEM	0.11	0.12	0.09	0.04	0.11	0.01	
	n	4	4	4	3	3	3	3
(+) -97	pKi	5.51	6.06	8.56	5.68	6.10	5.59	3
	SEM	0.02	0.18	0.06	0.02	0.07	0	
	n	3	3	2	3	3	3	1
(-)-97	pKi	5.45	5.33	6.81	5.47	5.71	5.51	3
	SEM	0.10	0.06	0.48	0.13	0.02	0.02	
	n	3	3	2	3	3	3	1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
98	pKi	5.96	6.52	8.32	6.45	6.23	6.37	3
	SEM	0.06	0.04	0.02	0.03	0.05	0.03	
	n	4	4	4	4	4	4	2
99	pKi	5.71	6.27	7.2	6.97	6.02	6.21	3
	SEM	0.03	0.13	0.32	0.02	0.01	0.05	
	n	3	3	3	2	2	2	2
100	pKi	5.31	5.83	8.36	6.10	5.54	5.75	3
	SEM	0.04	0.06	0.05	0.01	0.03	0.01	
	n	3	3	3	3	3	3	2
101	pKi	5.86	6.22	8.54	5.89	6.18	6.04	3
	SEM	0.08	0.04	0.04	0.02	0.06	0.04	
	n	4	4	4	4	4	4	2
(±)-102	pKi	5.46	5.79	8.42	5.54	5.99	5.76	4.14
	SEM	0.03	0.02	0.02	0.02	0.02	0.04	0.03
	n	4	4	4	3	3	3	2

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
(+) -102	pKi	5.54	5.91	8.58	5.41	5.72	5.48	3
	SEM	0.03	0.03	0.05	0.02	0.01	0.02	
	n	4	4	4	2	2	2	2
(-) -102	pKi	5.17	5.50	6.95	5.72	6.23	5.98	6.26
	SEM	0.10	0.02	0.03	0.02	0.01	0.01	0.05
	n	4	4	4	2	2	2	2
103	pKi	5.60	6.74	7.97	6.31	6.13	6.57	6.75
	SEM	0.03	0.08	0.04	0.02	0.07	0.06	0.12
	n	3	3	3	3	3	3	2
104	pKi	6.88	7.46	8.49	8.28	7.25	7.8	3
	SEM	0.02	0.03	0.04	0.06	0.08	0.02	
	n	3	3	3	3	3	3	2
105	pKi	5.61	5.50	6.16	5.90	5.66	5.86	5.18
	SEM	0.25	0.25	0.20	0.02	0.01	0.01	0.29
	n	3	3	3	4	4	4	2

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
106	pKi	5.62	6.03	7.82	6.49	6.43	6.53	3
	SEM	0.04	0.09	0.03	0.02	0.07	0.05	
	n	4	4	4	3	3	3	2
107	pKi	6.06	6.00	8.23				
	SEM	0.34	0.09	0.06				
	n	3	3	3				
108	pKi	5.53	5.38	8.16				
	SEM	0.07	0.06	0.31				
	n	3	3	3				
109	pKi	6.07	6.56	7.18				
	SEM	0.04	0.06	0.25				
	n	2	2	2				
110	pKi	4.75	4.50	5.81				
	SEM	0.13	0.14	0.48				
	n	3	3	3				

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
111	pKi	5.75	6.02	8.24				
	SEM	0.01	0.05	0.04				
	n	2	2	2				
112	pKi	7.52	7.63	7.61	6.59	6.35	6.57	7.24
	SEM	0.11	0.08	0.13	0.05	0.09	0.19	0.05
	n	3	3	3	3	3	3	2
113	pKi	6.16	6.46	7.75	6.12	6.78	6.50	3
	SEM	0.02	0.04	0.06	0.03	0.02	0.08	
	n	3	3	3	4	4	4	2
114	pKi	6.26	6.69	7.99	5.68	6.33	6.14	5.54
	SEM	0.13	0.05	0.04	0.04	0.03	0.04	0.1
	n	3	3	3	3	3	3	2
115	pKi	5.70	5.84	7.23	5.40	6.11	5.64	3
	SEM	0.01	0.13	0.05	0.06	0.03	0.03	
	n	3	3	3	3	3	3	2

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
116	pKi	6.73	6.12	8.41	5.84	6.43	6.13	
	SEM	0.44	0.09		0.16	0.07	0.01	
	n	2	2	1	3	3	3	
117	pKi	5.68	6.25	7.56	6.02	6.36	6.12	3
	SEM	0.12	0.04	0.05	0.06	0.03	0.05	
	n	3	3	3	3	3	3	2
118	pKi	5.66	5.75	8.02	5.41	5.84	5.65	3.00
	SEM	0.06	0.09	0.10	0.06	0.02	0.03	
	n	3	3	3	3	3	3	1
(±)-119	pKi	6.21	6.38	8.5	6.4	6.04	6.49	5.13
	SEM	0.08	0.03	0.09	0.07	0.02	0.02	0.11
	n	3	3	3	4	4	4	2
(+) -119	pKi	5.89	6.08	6.42				
	SEM	0.02	0.03	0.13				
	n	3	3	3				

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		alpha-1			alpha-2			Ca
		1a	1b	1c	2a	2b	2c	
(-)-119	pKi	5.93	6.17	8.59				
	SEM	0.02	0.03	0.12				
	n	3	3	3				
120	pKi	6.33	6.61	8.97	6.44	6.59	6.72	3
	SEM	0.05	0.04	0.09	0.03	0.02	0.03	
	n	4	4	4	3	3	3	3
121	pKi	6.62	7.14	8.88	6.44	6.59	6.72	4.78
	SEM	0.08	0.06	0.04	0.03	0.02	0.03	0.15
	n	3	3	3	3	3	3	2
122	pKi	6.62	7.57	7.71	6.38	7.35	6.53	3
	SEM	0.17	0.08	0.17	0.04	0.04	0	0
	n	4	4	4	3	3	3	1
123	pKi	6.7	8.01	8.3	6.03	6.87	6.42	4.53
	SEM	0.03	0.09	0.11	0.02	0.06	0.01	0
	n	4	4	4	3	3	3	1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
124	pKi	7.24	7.05	8.71	7.65	6.7	7.35	3
	SEM	0.06	0.17	0.05	0.02	0.04	0.02	0
	n	3	3	2	3	3	3	2
125	pKi	7.11	6.89	8.94	7.57	6.73	7.64	4.42
	SEM	0.09	0.06	0.08	0.07	0.03	0.05	0
	n	3	3	3	3	3	3	1
126	pKi	5.15	5.37	7.95	5.33	5.63	5.36	6.34
	SEM	0.02	0.01	0.06	0.04	0.02	0.01	0
	n	3	3	3	3	3	3	1
127	pKi	6.45	6.79	7.26	6.17	6.42	6.37	3
	SEM	0.01	0.09	0.01	0.01	0.05	0.03	0
	n	3	3	2	3	3	3	2
128	pKi	6.01	5.98	8.47	6.34	6.36	6.66	
	SEM	0.05	0.24	0.08	0.01	0.06	0.04	
	n	3	3	3	2	2	2	

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound		alpha-1			alpha-2			Ca
		1a	1b	1c	2a	2b	2c	
129	pKi	6.17	6.29	8.43				4
	SEM	0.08	0.23	0.25				
	n	2	2	2				1
130	pKi	6.04	6.38	7.97				
	SEM	0.29	0.23	0.1				
	n	3	3	3				
131	pKi	5.83	6.07	8.34				4
	SEM	0.35	0.27	0.47				
	n	4	4	3				1
132	pKi	6.11	6.41	7.24				4.1
	SEM	0.06	0.19	0.45				
	n	4	4	3				1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
135	PKi	6.30	6.75	6.98	6.18	6.41	6.47	
	SEM	0.20	0.16	0.12				
	n	3	3	2	1	1	1	
136	PKi	6.08	6.39	8.46				
	SEM	0.16	0.12	0.04				
	n	3	3	2				
139	PKi	6.32	6.85	7.63	6.08	5.90	6.51	
	SEM	0.18	0.11	0.13	0.05	0.05	0.01	
	n	3	3	3	2	2	2	
140	PKi	5.14	4.84	5.15				
	SEM							
	n	1	1	1				
141	PKi	7.30	7.48	8.27	6.22	6.36	6.45	
	SEM	0.01	0.09	0.04	0.07	0.14	0.01	
	n	2	2	2	3	3	3	

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
143	PKi	6.50	6.92	8.49				
	SEM	0.07	0.09	0.07				
	n	2	2	2				
(\pm)-144	PKi	6.20	6.49	9.19	6.40	6.05	6.69	4.90
	SEM	0.05	0.05	0.12	0.03	0.04	0.03	
	n	4	4	4	2	2	3	1
145	PKi	6.42	6.49	8.21				
	SEM							
	n	1	1	1				
146	PKi	5.73	5.92	8.43				
	SEM	0.28	0.32	0.27				
	n	2	2	2				
147	PKi	6.43	6.59	7.96	6.06	5.96	6.60	
	SEM	0.13	0.11	0.14				
	n	2	2	2	1	1	1	

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
148	PKi	6.34	5.59	8.53				
	SEM	0.07	0.06	0.09				
	n	2	2	2				
149	PKi	6.49	6.61	8.26	6.30	6.25	6.59	
	SEM	0.03	0.00		0.05	0.04	0.06	
	n	2	2	1	2	2	2	
150	PKi	6.61	6.84	8.77				
	SEM	0.03	0.43	0.12				
	n	2	2	2				
151	PKi	6.20	6.45	7.91	6.25	6.27	6.68	
	SEM	0.06	0.06	0.03				
	n	3	3	3	1	1	1	
152	PKi	6.31	6.66	6.03				
	SEM	0.13	0.04	0.09				
	n	2	2	2				

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
153	PKI	5.72	6.42	7.62				
	SEM	0.01	0.08	0.01				
	n	2	2	2				
154	PKI	6.95	7.06	8.74				
	SEM	0.01	0.02	0.15				
	n	2	2	2				

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
156	PKI	5.88	6.17	7.02	6.50	6.25	6.66	4.12
	SEM	0.02	0.06	0.12				
	n	4	4	4	1	1	1	1
157	PKI	6.42	6.74	8.42	6.02	6.30	6.36	5.26
	SEM	0.04	0.04	0.16	0.03	0.05	0.02	
	n	3	3	3	2	2	2	1
158	PKI	6.42	6.90	7.81				
	SEM	0.20	0.12	0.09				
	n	3	3	3				
159	PKI	6.41	6.75	8.30				5.78
	SEM	0.03	0.05	0.13				
	n	4	4	4				1
160	PKI	6.60	6.86	8.10	6.34	6.83	6.81	4.81
	SEM	0.03	0.04	0.14				
	n	4	4	4	1	1	1	1
161	PKI	5.88	6.39	7.41				3.00
	SEM	0.08	0.10	0.04				
	n	4	4	4				1
162	PKI	5.97	6.59	7.94	6.20	6.46	6.26	4.30
	SEM	0.03	0.05	0.03	0.01	0.01	0.00	0.10
	n	3	3	3	2	2	2	2

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
163	PKI	6.11	5.99	7.73	5.93	5.77	5.91	
	SEM	0.01	0.04	0.07	0.02	0.20	0.21	
	n	3	3	3	2	2	2	
164	PKI	5.53	5.75	7.64				
	SEM	0.02	0.09	0.03				
	n	3	3	3				
165	PKI	5.85	6.24	9.30	5.52	5.71	5.82	
	SEM	0.06	0.05	0.26	0.06	0.01	0.02	
	n	4	4	4	2	2	2	
166	PKI	5.63	5.88	8.89	5.73	5.41	5.99	3.88
	SEM	0.02	0.08	0.15	0.02	0.02	0.03	
	n	3	3	3	4	4	4	1
167	PKI	6.50	6.57	8.36				3.00
	SEM	0.14	0.05	0.04				0.00
	n	3	3	3				2
168	PKI	6.36	6.74	8.42				3.77
	SEM	0.21	0.02	0.10				0.13
	n	3	3	3				2
169	PKI	6.29	6.64	8.14				3.00
	SEM	0.24	0.05	0.13				0.00
	n	3	3	3				2

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
170	PKI	6.53	6.98	8.90	5.21	5.06	5.31	5.62
	SEM	0.04	0.05	0.14	0.54	0.57	0.84	0.17
	n	3	3	3	2	2	2	2
171	PKI	5.98	6.21	8.76	5.96	5.70	6.24	4.73
	SEM	0.03	0.16	0.13	0.02	0.06	0.02	
	n	3	3	3	2	2	2	1
172	PKI	6.09	6.21	8.55	5.63	5.46	6.16	
	SEM	0.53	0.10	0.03	0.08	0.04	0.03	
	n	3	3	2	2	2	2	
173	PKI	6.13	6.37	8.40	6.57	6.02	5.83	
	SEM	0.08	0.01	0.11	0.00	0.08	0.08	
	n	3	3	2	2	2	2	
174	PKI	5.40	5.72	8.39	5.70	6.02	6.17	
	SEM	0.04	0.03	0.16				
	n	3	3	3	1	1	1	
175	PKI	6.34	6.46	8.29	6.97	6.66	6.52	
	SEM	0.02	0.08	0.04				
	n	3	3	3	1	1	1	
176	PKI	6.51	6.80	8.43	6.01	5.92	6.14	
	SEM	0.04	0.07	0.15	0.04	0.07	0.11	
	n	3	3	3	2	2	2	

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
177	PKI	5.85	6.12	8.33	5.78	5.54	6.08	4.03
	SEM	0.06	0.05	0.09	0.13	0.07	0.02	
	n	4	4	4	2	2	2	1
178	PKI	6.08	6.38	8.59	6.04	6.12	6.40	
	SEM	0.04	0.08	0.05	0.15	0.16	0.03	
	n	3	3	3	2	2	2	
179	PKI	5.38	5.97	8.48	5.48	5.73	5.84	3.00
	SEM	0.07	0.16	0.10	0.01	0.04	0.00	
	n	3	3	3	2	2	2	1
180	PKI	5.52	6.07	8.44	5.16	5.44	5.24	3.00
	SEM	0.06	0.09	0.10	0.07	0.18	0.45	
	n	3	3	3	2	2	2	1
181	PKI	5.46	5.97	8.39				3.00
	SEM	0.04	0.03	0.05				
	n	3	3	3				1
182	PKI	5.47	5.95	8.65	5.66	6.04	5.94	3.45
	SEM	0.04	0.08	0.05	0.16	0.07	0.04	0.29
	n	3	3	3	2	2	2	2
183	PKI	6.30	6.64	9.07	5.98	6.14	6.36	4.13
	SEM	0.02	0.05	0.10	0.06	0.01	0.08	0.35
	n	3	3	3	2	2	2	2

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
184	PKI	6.13	6.76	8.02				4.91
	SEM	0.06	0.13	0.08				0.27
	n	3	2	2				3
185	PKI	5.72	6.03	8.50	6.56	5.89	6.45	3.23
	SEM	0.08	0.10	0.03	0.02	0.03	0.11	
	n	4	4	4	3	3	3	2
186	PKI	5.68	6.32	8.20	6.45	5.80	6.58	5.19
	SEM	0.12	0.14	0.06	0.08	0.10	0.03	0.05
	n	3	3	3	2	2	2	2
187	5.15	5.29	6.27	8.46	5.91	5.65	5.29	3.29
	SEM	0.06	0.10	0.09	0.22	0.07	0.02	0.14
	n	3	3	3	3	3	3	2
188	PKI	5.25	5.41	8.21				3.00
	SEM	0.08	0.04	0.01				0.00
	n	3	3	3				2
189	PKI	5.33	5.85	7.58				
	SEM	0.09	0.26	0.05				
	n	3	3	3				
190	PKI	5.87	6.15	8.27				
	SEM	0.03	0.03	0.11				
	n	3	3	3				

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
191	PKI	5.71	5.87	8.09				
	SEM	0.10	0.14	0.08				
	n	3	3	3				
192	PKI	5.52	5.73	8.51	5.43	5.21	5.83	
	SEM	0.01	0.02	0.11	0.08	0.01	0.04	
	n	3	3	3	2	2	2	
193	PKI	5.54	5.76	8.80	5.99	5.62	6.20	
	SEM	0.01	0.04	0.07	0.05	0.10	0.07	
	n	3	3	3	2	2	2	
194	PKI	5.31	5.57	8.43	5.50	5.24	5.97	
	SEM	0.05	0.02	0.08	0.04	0.00	0.04	
	n	4	4	4	2	2	2	
195	PKI	6.54	6.89	8.15				
	SEM	0.01	0.09	0.06				
	n	4	4	4				
196	PKI	5.17	5.44	7.41	5.08	5.33	5.51	
	SEM	0.11	0.05	0.10	0.12	0.14	0.09	
	n	3	3	3	2	2	2	
197	PKI	6.60	6.83	9.26	5.83	5.63	6.29	5.20
	SEM	0.01	0.02	0.11	0.09	0.01	0.12	
	n	4	4	4	2	2	2	1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
198	PKI	5.35	5.56	9.08	5.95	5.97	5.61	3.75
	SEM	0.02	0.04	0.09	0.19	0.02	0.01	
	n	4	4	4	3	3	3	1
199	PKI	5.30	5.57	8.55	5.65	6.04	5.56	3.58
	SEM	0.03	0.04	0.09	0.09	0.03	0.08	
	n	4	4	4	3	3	3	1
200	PKI	5.48	5.70	8.36	5.26	5.97	5.79	3.00
	SEM	0.05	0.04	0.06	0.04	0.02	0.02	
	n	3	3	3	2	2	2	1
201	PKI	5.65	5.93	8.59	5.35	5.92	5.49	4.17
	SEM	0.01	0.05	0.05	0.02	0.09	0.08	0.01
	n	3	3	3	2	2	2	2
202	PKI	5.66	5.85	8.57	5.35	6.04	5.67	3.58
	SEM	0.04	0.09	0.10	0.08	0.00	0.04	0.29
	n	3	3	3	2	2	2	2
202-	PKI	5.81	5.87	8.79				
	SEM	0.06	0.11	0.08				
	n	2	2	2				
202+	PKI	5.79	5.81	8.02				
	SEM	0.08	0.02	0.02				
	n	2	2	2				

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
203	PKI	6.12	6.28	8.32				
	SEM	0.03	0.04	0.04				
	n	3	3	3				
204	PKI	4.54	4.54	7.23	5.93	5.77	5.91	
	SEM	0.03	0.04	0.21				
	n	3	3	3	1	1	1	
205	PKI	5.32	5.51	8.32				
	SEM	0.03	0.04	0.08				
	n	3	3	3				
206	PKI	5.94	6.16	8.44				
	SEM	0.05	0.08	0.12				
	n	3	3	3				
207	PKI	5.73	5.83	8.62	6.14	6.02	5.75	
	SEM	0.06	0.07	0.10	0.12	0.05	0.08	
	n	3	3	3	2	2	2	
208	PKI	6.13	6.41	8.43	5.57	5.90	6.01	
	SEM	0.13	0.08	0.17	0.03	0.02	0.01	
	n	3	3	3	2	2	2	
209	PKI	5.17	5.44	8.41	5.78	6.46	5.70	4.53
	SEM	0.02	0.04	0.16	0.02	0.07	0.02	
	n	3	3	3	2	2	2	1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
210	PKI	4.14	4.35	7.03	4.96	4.63	4.66	6.03
	SEM	0.00	0.01	0.13	0.12	0.09	0.09	
	n	2	2	2	3	3	3	1
211	PKI	5.50	5.80	8.27	5.58	5.68	5.71	
	SEM	0.02	0.11	0.04	0.01	0.00	0.06	
	n	3	3	3	2	2	2	
212	PKI	4.95	5.27	8.03	5.58	5.57	5.44	
	SEM	0.03	0.04	0.08	0.05	0.05	0.04	
	n	3	3	3	2	2	2	
213	PKI	6.23	6.81	8.22	6.00	6.70	5.75	
	SEM	0.04	0.08	0.02	0.02	0.05	0.16	
	n	3	3	3	2	2	2	
214	PKI	5.59	6.11	8.21				
	SEM	0.04	0.10	0.03				
	n	3	3	3				
215	PKI	5.47	5.90	8.44				
	SEM	0.09	0.15	0.06				
	n	3	3	3				
216	PKI	7.22	8.15	8.77				6.00
	SEM	0.07	0.13	0.08				
	n	3	3	3				1

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		alpha-1			alpha-2			Ca
		1a	1b	1c	2a	2b	2c	
217	PKI	6.11	6.35	8.61				5.09
	SEM	0.17	0.15	0.11				0.11
	n	4	3	3				2
218	PKI	6.78	7.75	8.86				4.12
	SEM	0.05	0.15	0.11				0.56
	n	3	3	3				2
219	PKI	5.57	5.91	7.52				3.24
	SEM	0.01	0.08	0.04				0.12
	n	3	3	3				2
220	PKI	5.67	6.28	8.01				3.36
	SEM	0.06	0.09	0.08				0.18
	n	4	4	4				2
221	PKI	6.73	7.28	8.21				4.85
	SEM	0.02	0.07	0.07				0.07
	n	4	4	4				3
222	PKI	4.85	5.17	7.38				3.55
	SEM	0.05	0.06	0.04				0.13
	n	4	4	4				3
223	PKI	6.05	6.76	7.46				3.56
	SEM	0.04	0.05	0.05				0.28
	n	4	4	4				2

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
224	PKI	6.18	6.58	8.16				4.82
	SEM	0.02	0.05	0.11				0.13
	n	3	3	3				2
225	PKI	5.79	6.30	8.40	5.69	5.60	6.38	5.59
	SEM	0.04	0.01	0.17	0.15	0.13	0.18	0.08
	n	3	3	3	2	2	2	3
226	PKI	6.65	7.01	7.96				5.06
	SEM	0.05	0.03	0.07				0.04
	n	3	3	3				2
227	PKI	5.29	5.58	7.63				4.15
	SEM	0.03	0.04	0.07				0.21
	n	3	3	3				2
228	PKI	5.46	5.83	7.78				4.47
	SEM	0.13	0.12	0.20				0.10
	n	3	3	3				2
229	PKI	5.38	5.86	8.15	5.52	5.27	6.05	4.00
	SEM	0.05	0.04	0.01	0.09	0.07	0.07	0.04
	n	3	3	3	2	2	2	2
230	PKI	5.75	6.16	8.06				5.04
	SEM	0.05	0.11	0.16				0.10
	n	3	3	3				2

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
231	PKI	5.91	6.30	8.36				3.41
	SEM	0.03	0.03	0.14				0.20
	n	3	3	2				2
232	PKI	6.38	6.66	8.12				6.16
	SEM	0.18	0.16	0.03				
	n	2	2	2				1
233	PKI	5.39	5.79	8.67	5.32	5.06	5.78	6.59
	SEM	0.03	0.04	0.04	0.03	0.01	0.03	
	n	2	2	2	2	2	2	1
234	PKI	5.56	5.89	8.79	5.91	5.31	6.08	3.40
	SEM	0.03	0.07	0.18	0.04	0.01	0.00	0.12
	n	3	3	3	2	2	2	2
235	PKI	6.55	6.66	8.68	5.62	5.53	5.99	3.78
	SEM	0.03	0.01	0.12	0.01	0.05	0.01	0.23
	n	3	3	3	2	2	2	3
236	PKI	6.46	6.69	8.60				
	SEM	0.02	0.08	0.02				
	n	3	3	3				
237	PKI	6.42	6.70	8.58	6.10	6.07	6.49	
	SEM	0.03	0.06	0.02				
	n	3	3	3	1	1	1	

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		α -1			α -2			Ca
		1a	1b	1c	2a	2b	2c	
238	PKI	6.08	6.25	8.55	6.17	6.05	6.60	
	SEM							
	n	1	1	1	1	1	1	
239	PKI	6.56	6.59	8.69	6.08	6.12	6.58	
	SEM							
	n	1	1	1	1	1	1	
240	PKI	5.00	5.35	7.57	4.73	5.20	4.93	
	SEM							
	n	1	1	1	1	1	1	
241	PKI	5.84	6.31	8.36	5.80	5.93	6.40	
	SEM							
	n	1	1	1	1	1	1	
242	PKI	6.65	7.08	8.40	5.85	6.03	6.59	
	SEM							
	n	1	1	1	1	1	1	
243	PKI	5.82	6.12	8.24	5.65	6.01	5.97	
	SEM							
	n	1	1	1	1	1	1	
244	PKI	6.07	6.29	8.46	5.99	5.67	7.01	
	SEM							
	n	1	1	1	1	1	1	

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Table 1. Binding Affinities at α -Adrenergic Receptors and L-Type Calcium Channels

compound (synonym)		alpha-1			alpha-2			Ca
		1a	1b	1c	2a	2b	2c	
245	PKI	6.01	6.45	8.30	5.98	5.56	6.50	
	SEM							
	n	1	1	1	1	1	1	
246	PKI	6.50	6.76	8.56	6.17	6.51	5.62	
	SEM							
	n	1	1	1	1	1	1	
247	PKI	6.01	6.04	7.61	6.23	6.32	6.52	
	SEM							
	n	1	1	1	1	1	1	
248	PKI	5.53	5.82	6.76	6.00	5.94	6.28	
	SEM							
	n	1	1	1	1	1	1	
249	PKI	6.37	6.63	9.41	5.81	5.91	6.25	7.51
	SEM	0.03	0.09	0.09	0.06	0.02	0.03	0.12
	n	3	3	2	3	3	3	3
250	PKI	6.22	7.16	8.96	6.91	7.40	7.44	4.88
	SEM	0.41	0.06	0.12	0.05	0.04	0.06	
	n	3	3	3	2	2	2	1
251	PKI	5.49	4.49	5.47				
	SEM	0.10	0.00	0.10				
	n	2	2	2				

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Several of the compounds of the invention showed *in vitro* efficacy in blocking the contraction of the human prostate induced by phenylephrine, a selective α_1 -adrenergic agonist. The protocol for these experiments is given below. Table 2 shows the results.

Functional Properties of α_1 Antagonists in the Human Prostate

The efficacy of α_1 adrenergic antagonists for the treatment of benign prostatic hyperplasia (BPH) is related to their ability to elicit relaxation of prostate smooth muscle. An index of this efficacy can be obtained by determining the potency of α_1 antagonists to antagonize the contraction of human prostatic tissue induced by an α_1 agonist "in vitro". Furthermore, by comparing the potency of subtype selective α_1 antagonists in binding assays using human α_1 receptors with their potency to inhibit agonist-induced smooth muscle contraction, it is possible to determine which of the α_1 adrenergic receptor subtypes is involved in the contraction of prostate smooth muscle.

Methods: Prostatic adenomas were obtained at the time of surgery from patients with symptomatic BPH. These were cut into longitudinal strips of 15mm long and 2-4 mm wide, and suspended in 5ml organ baths containing Krebs buffer (pH 7.4). The baths were maintained at 37°C and continuously oxygenated with 5% CO₂ and 95% O₂. Isometric tension was measured with a Grass Instrument FT03 force transducer interfaced with a computer. Tissue strips were contracted with varying concentrations of phenylephrine after incubating for 20 minutes in the absence and presence of at least three different concentrations of antagonist. Dose-response curves for phenylephrine were constructed, and the antagonist potency (pA₂) was estimated by the dose-ratio method. The concentration of some antagonists in the tissue bath was

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assessed by measuring the displacement of [3H]prazosin by aliquots of the bath medium, using membrane preparations of the cloned human α_{1c} receptor. This control was necessary to account for losses of antagonist due to
5 adsorption to the tissue bath and/or metabolism during the time the antagonists were equilibrated with the prostate tissue.

Table 2. In Vitro Human Prostate Model

10

<u>Compound</u>	<u>pK_i</u>
(±)-2	9.23 ± 0.18
(±)-45	8.07 ± 0.13
15 (±)-93	7.28 ± 0.4

Several of the compounds of the invention showed *in vivo* efficacy in blocking the contraction of the canine
20 prostate induced by phenylephrine. The protocol for these experiments is given below. Table 3 shows the results (Diane Felsen, et. al. The Journal of Urology 1989, 141, 1230-1233).

25 **Protocol for In Vivo Evaluation of Compounds in Canine Prostate**

Adult male mongrel dogs more than one year of age were chosen for the model. After induction of general
30 anesthesia using sodium pentobarbital (25 mg/Kg i.v.), the animals were intubated and allowed to breathe spontaneously. An arterial catheter was inserted via the femoral artery to monitor blood pressure and i.v. line was inserted into the leg for fluid and drug
35 administration. A constant saline infusion was maintained at 40 to 50 mL/h. Next, a seven cm lower abdominal incision was made one cm lateral to the penis.

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The bladder, prostate and a short segment of urethra were identified and isolated, without damage to the nerves or blood vessels. A cystotomy incision was made through which the pressure catheter was inserted and positioned
5 in the prostatic urethra. The cystotomy was not closed, but the wound edges were sutured to stop bleeding. The tip of the catheter was positioned just distal to the prostate and secured in place with an O-silk tie around the urethra. A second holding suture at the bladder neck
10 secured the catheter in place.

An esophageal pressure catheter (Arndorfer Med. Spec. Inc., Greendale, WI), used to measure closing pressures along the esophagus was easily adoptable to our
15 study. Fluid, either water or saline, was pumped by a Harvard infusion pump at 0.1 mL/min through a Gould pressure transducer into the catheter. The fluid exists at a port in the catheter which is in the prostatic urethra. Occlusion of the port, by contraction of the
20 prostate, blocks the flow and a pressure wave is created. This pressure is transmitted back through the catheter to the transducer which is attached to a Gould recorder. Squeezing the prostate gland caused an increase in urethral pressure which verified the correct position in
25 the urethra.

The compounds were tested as follows: A dose response curve was first generated for phenylephrine alone, in doses ranging from one $\mu\text{g/Kg}$ to 50 $\mu\text{g/Kg}$. The
30 absolute rise in urethral pressure was recorded for each dose and the next dose given when the urethral pressure returned to baseline. Phenylephrine dose response curves were generated in all animals tested. Increasing doses of compounds were then given, and the phenylephrine dose
35 response curve repeated in the prepense of each dose of the compound. No animal received more than one compound; four animals were used to test each compound. To test

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for tachyphylaxis, four separate dogs were challenged with repeated phenylephrine doses for six hrs, the usual length of each experiment. From the dose-effect data, the inhibition constant (K_i) and the median-effect dose (ED₅₀) were calculated. Both the K_i and ED₅₀ values given are calculated by using microcomputer software and an IBM-PC.

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Table 3. In Vivo Dog Prostate Model

5	<u>Compound</u>	<u>K_i (nmol/Kg)</u>
	(±)-2	1.9
	(±)-45	12
10	(±)-93	7.6

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Table 4

Potency of Selected α_1 Antagonists to Block
Phenylephrine-Induced Contraction of Human Prostate

	<u>Compound</u>	<u>pA2</u>
5	(+) - 102	10.43 \pm 0.14
	97	9.12 \pm 0.13
10	38	8.98 \pm 0.06
	42	8.92 \pm 0.08
15	81	8.60 \pm 0.03
	73	8.56 \pm 0.07
	128	8.21 \pm 0.06
20		

Table 5

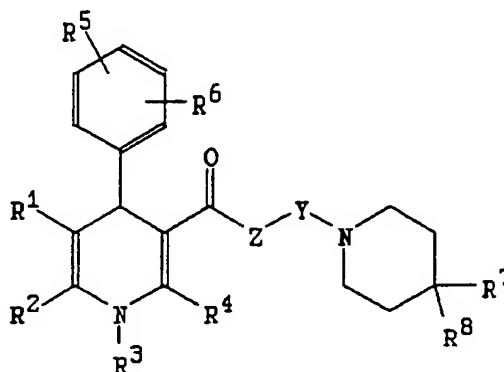
Ability of Selected α_1 Antagonists to Inhibit
Phenylephrine-Induced Increases in Urethral Pressure
and Arterial Pressure in Anesthetized Dogs

	<u>Compound</u>	<u>Urethral Pressure</u> <u>K_i</u> <u>(nmol/kg)</u>
25		
30	97	10 \pm 2.0
	42	9 \pm 2.5
35	38	8 \pm 1.5

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What is claimed is:

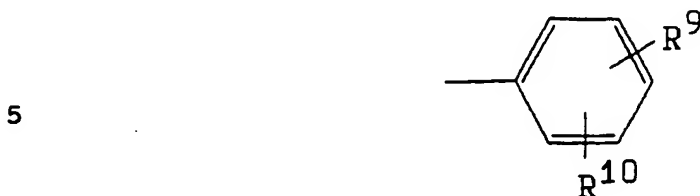
1. A method of treating benign prostatic hyperplasia in a subject which comprises administering to the subject a therapeutically effective amount of a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH or CH_2 ; wherein R^1 is a linear or branched chain alkyl, alkoxyalkyl or arylalkyl group; wherein R^2 and R^4 are independently the same or different and are H, or a linear or branched chain alkyl group; wherein R^3 is H, a linear or branched chain alkyl, alkoxy, alkoxyalkyl or acyl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , N_3 , CN, CF_3 or NH_2 , or a linear or branched chain alkyl, alkoxy, alkoxyalkyl, alkoxyalkyl, acyl, alkylsulfoxide, alkylsulfone or mono- or dialkylamino group; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR, OCOR, NH_2 , NHR, NR_2 , or NHCOR, where R is a linear chain alkyl group, a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl, or thiophene

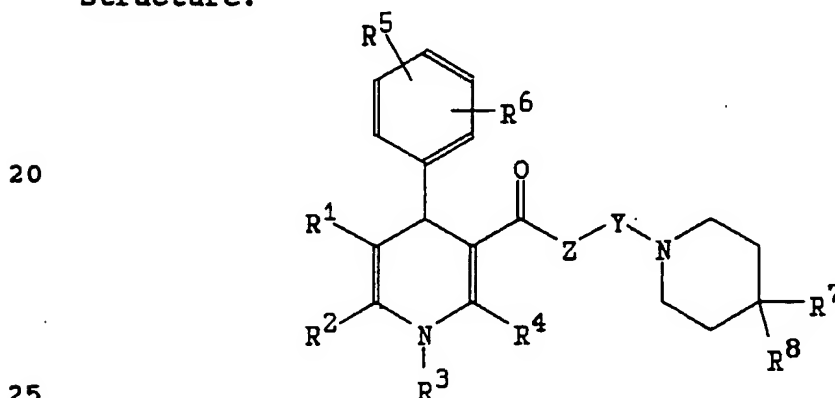
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group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, F, OH, OR', OCOR', OCOOR', OCONHR',
 10 NH_2 , NHR', NR', NHCOR', NHCOOR' or NHCONHR', where R' is a linear or branched chain alkyl group.

2. A method of lowering intraocular pressure in a subject which comprises administering to the subject a
 15 therapeutically effective amount of a compound having the structure:

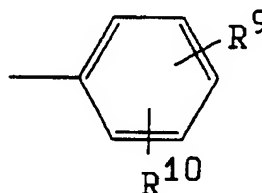


wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O,
 30 NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^1 is a linear or branched chain alkyl, alkoxyalkyl or arylalkyl group; wherein R^2 and R^4 are independently the same or different and are H, or a
 35 linear or branched chain alkyl group; wherein R^3 is H, a linear or branched chain alkyl, alkoxy, alkoxyalkyl or acyl group; wherein R^5 and R^6 are independently the same

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or different and are H, OH, Cl, Br, I, F, NO₂, N₃, CN, CF₃, or NH₂, or a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfone or mono- or dialkylamino group; wherein R⁷ and R⁸ are
 5 independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂ or NHCOR', where R' is a linear chain alkyl group, or a benzyl group, or are a linear or branched chain alkyl or cycloalkyl group, a heteroaryl group comprising a pyridyl, indolyl,
 10 indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:

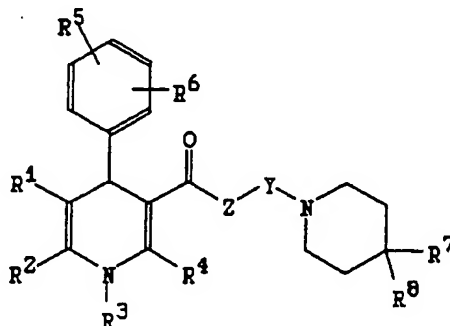
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wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, F, OH, OR'', OCOR'', OCOOR'',
 20 OCONHR'', NH₂, NHR'', NR''₂, NHCOR'', NHCOOR'' or NHCONHR'', where R'' is a linear or branched chain alkyl group.

3. A method of inhibiting cholesterol synthesis in a
 25 subject which comprises administering to the subject a therapeutically effective amount of a compound having the structure:

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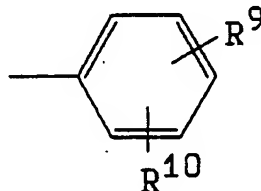
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wherein A is CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; Y is -(CH₂)_n-,

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where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$ where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein R¹ is a linear or branched chain alkyl, alkoxyalkyl or arylalkyl group; wherein R² and R⁴ are independently the same or different and are H, or a linear or branched chain alkyl group; wherein R³ is H, a linear or branched chain alkyl, alkoxy, alkoxyalkyl or acyl group; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, F, NO₂, CN, CF₃ or NH₂, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone or mono- or dialkylamino group; and wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR'', OCOR'', NH₂, NHR'', NR''₂, or NHCOR'', where R'' is a linear chain alkyl group, a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

25



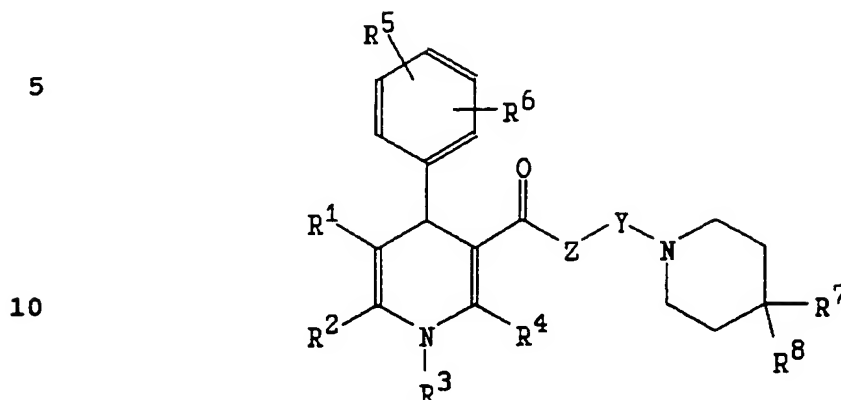
30 wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, F, OH, OR''', OCOR''', OCOOR''', OCONHR''', NH₂, NHR''', NR'''₂, NHCOR''', NHCOOR''' or NHCONHR''', where R''' is a linear or branched chain alkyl group.

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4. A method of treating diseases mediated by α_1 receptors in a subject which comprises administering to the subject

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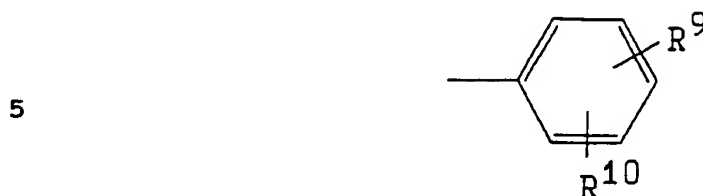
a therapeutically effective amount of a compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^1 is a linear or branched chain alkyl, alkoxyalkyl or arylalkyl group; wherein R^2 and R^4 are independently the same or different and are H, or a linear or branched chain alkyl group; wherein R^3 is H, a linear or branched chain alkyl, alkoxy, alkoxyalkyl or acyl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, F, NO_2 , CN, CF_3 or NH_2 , or a linear or branched chain alkyl, alkoxy, alkoxy-carbonyl, acyl, alkylsulfoxide, alkylsulfone or mono- or dialkylamino group; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR'' , $OCOR''$, NH_2 , NHR'' , NR''_2 or $NHCOR''$, where R'' is a linear chain alkyl group, a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or

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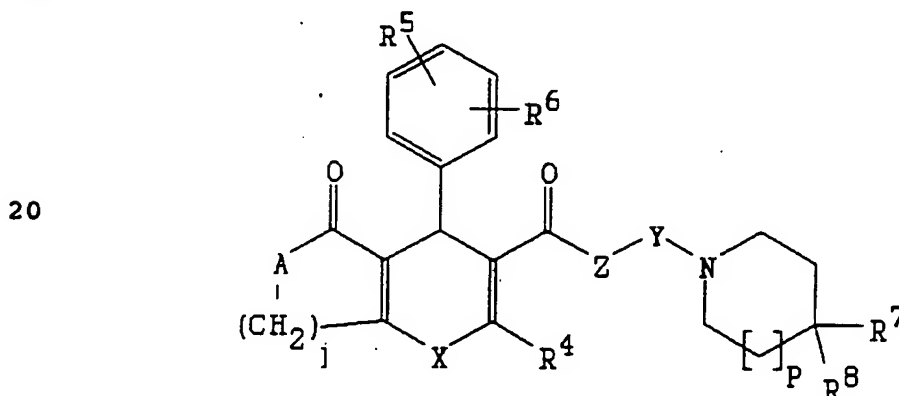
thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, F, OH, OR''', OCOR''', OCOOR''',
 10 OCONHR''', NH_2 , NHR''', NR'''_2 , NHCOR''', NHCOOR''' or NHCONHR''', where R''' is a linear or branched chain alkyl group.

5. A compound having the structure:

15

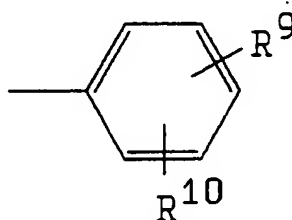


25

wherein A and X are independently the same or different and are CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$,
 30 where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH_2 , where R' is a methyl, ethyl or propyl group;
 35 wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R^4 is H, a linear, cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-

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alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or
 5 an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is
 10 a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , N_3 or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl,
 15 alkylsulfoxide, alkylsulfone, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' ,
 20 $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the
 25 structure:

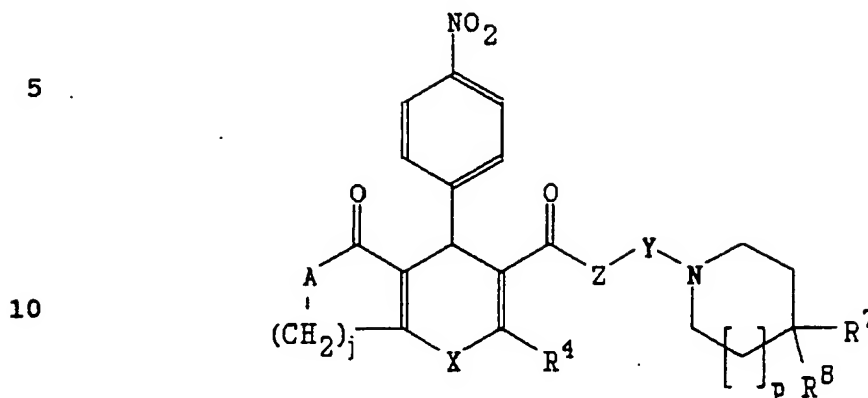


30

wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$,
 35 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

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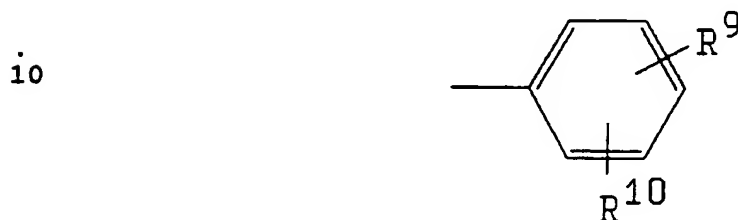
6. The compound of claim 5, wherein the compound has the structure:



wherein A and X are independently the same or different
 15 and are CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where
 R is a methyl, ethyl or propyl group; wherein Y is -
 $(\text{CH}_2)_n$ -, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h\text{-O-}(\text{CH}_2)_k$ -,
 where h and k are independently the same or different and
 are 2, 3 or 4; $-(\text{CH}_2)_h\text{-CH=CH-}(\text{CH}_2)_k$ -; or $-(\text{CH}_2)_h\text{-C}\equiv\text{C-}(\text{CH}_2)_k$ -,
 20 where h and k are independently the same or different and
 are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' ,
 NOR' or CH_2 , where R' is a methyl, ethyl or propyl group;
 wherein p is 0, 1 or 2; wherein R^4 is H, a linear, cyclic
 or branched chain alkyl, an alkoxyalkyl, azidoalkyl,
 25 aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl,
 aminoalkyl, hydroxyalkyl or an aryl group, or $(\text{CH}_2)_t\text{W}$,
 where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 ,
 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl
 30 group, or an aryl group, where R' is a linear or branched
 chain alkyl group, or an aryl group, where W^0 is O , S or
 NH , W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 ,
 and where R' is a linear or branched chain alkyl group,
 or an aryl group, where Z^- is a pharmaceutically
 35 acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v
 is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently
 the same or different and are H, CN, CF_3 , OH, OR' , OCOR' ,

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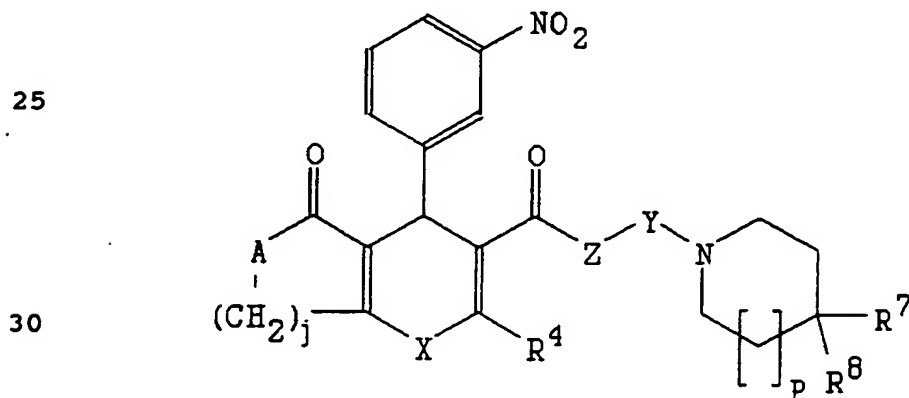
NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH ,
 COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$,
 or a benzyl group, a linear or branched chain alkyl or
 cycloalkyl group, or are a heteroaryl group comprising a
 5 pyridyl, indolyl, indolylalkyl, quinolinyl, isoquin-
 olinyl, pyrrol, furyl or thiophene group, or an aryl
 group having the structure:



wherein R^9 and R^{10} are independently the same or different
 15 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} ,
 $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 where R' is a linear or branched chain alkyl group, and
 R^{iv} is a linear or branched chain alkyl group, and q is 2,
 3, 4 or 5.

20

7. The compound of claim 5, wherein the compound has the structure:



wherein A and X are independently the same or different
 and are CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S, where
 35 R is a methyl, ethyl or propyl group; wherein Y is -
 $(\text{CH}_2)_n$ -, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h\text{-O}-(\text{CH}_2)_k$ -,
 where h and k are independently the same or different and

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are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group;

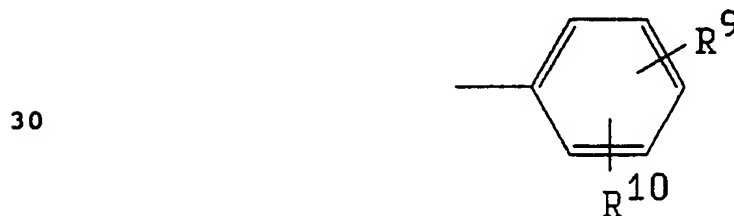
5 wherein j is 1 or 2; wherein p is 0 or 2; wherein R⁴ is H, a linear, cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_tW$, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻,

10 , NHCOR', N₃, NO₂, or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR',

15 N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃,

20 OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,

25 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



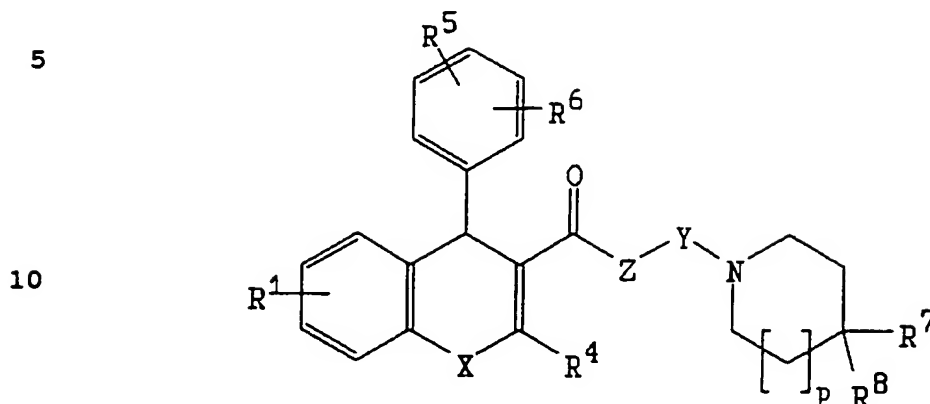
wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR₂^{iv}, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv},

35 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group and q is 2,

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3, 4 or 5.

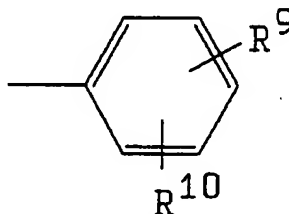
8. A compound having the structure:



wherein X is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S ,
 15 where R is a methyl, ethyl or propyl group; wherein Y is
 $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$,
 where h and k are independently the same or different and
 are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$,
 where h and k are independently the same or different and
 20 are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' ,
 NOR' or CH_2 , where R' is a methyl, ethyl or propyl group;
 wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R^1 is
 H , Cl , Br , I , F , NO_2 , CN , OH , OR'^2 , OCOR'^2 , NH_2 , NR'^2 ,
 NHCOR'^2 , or CF_3 , where R'^2 is a linear or branched chain
 25 alkyl group, or an aryl group; wherein R^4 is H , a linear,
 cyclic or branched chain alkyl, an alkoxyalkyl, azido-
 alkyl, aminoalkoxyalkyl, azidoalkoxyalkyl,
 trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl
 group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$,
 NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched
 30 chain alkyl group, or an arylalkyl group, or an alkenyl
 or alkynyl group, or an aryl group, where R' is a linear
 or branched chain alkyl group, or an aryl group, where W^0
 is O , S or NH , W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' ,
 35 N_3 or NO_2 , and where R' is a linear or branched chain
 alkyl group, or an aryl group, where Z^- is a
 pharmaceutically acceptable counterion, and t is 1, 2, 3,

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4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , N_3 or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

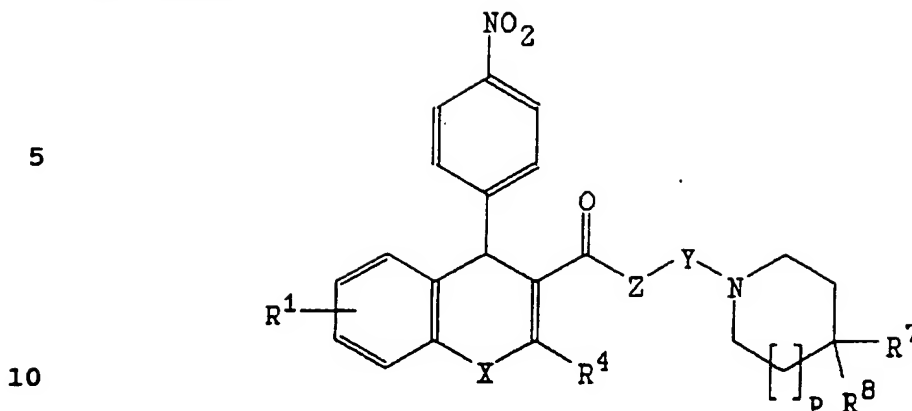


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group and q is 2, 3, 4 or 5.

9. The compound of claim 8, wherein the compound has the

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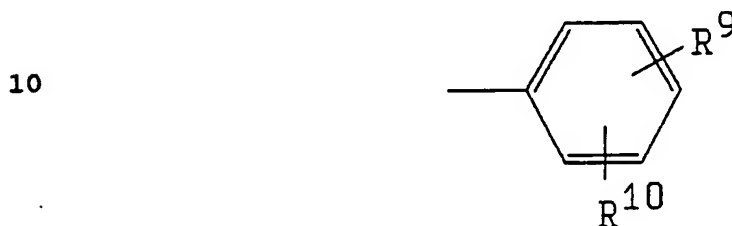
structure:



wherein X is CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R¹ is H, Cl, Br, I, F, NO₂, CN, OH, OR''², OCOR''², NH₂, NR''², NHCOR''², or CF₃, where R''² is a linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, a linear, cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_jW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃,

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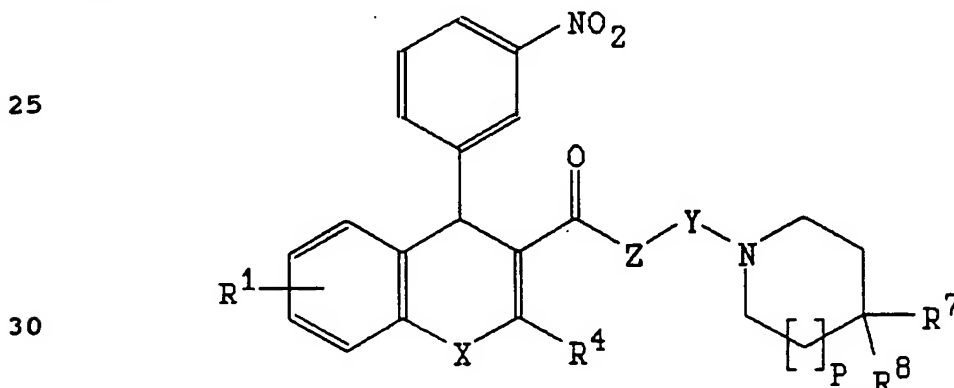
OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR',
 CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH
 or COO(CH₂)_qOR', or a benzyl group, a linear or branched
 chain alkyl or cycloalkyl group, or are a heteroaryl
 5 group comprising a pyridyl, indolyl, indolylalkyl,
 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 15 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv},
 OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv},
 where R' is a linear or branched chain alkyl group, and
 R^{iv} is a linear or branched chain alkyl group and q is 2,
 3, 4 or 5.

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10. The compound of claim 8, wherein the compound has
 the structure:

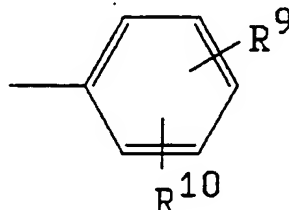


wherein X is CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S,
 where R is a methyl, ethyl or propyl group; wherein Y is
 35 -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-,
 where h and k are independently the same or different and
 are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-,

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where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R¹ is
 5 H, Cl, Br, I, F, NO₂, CN, OH, OR'', OCOR'', NH₂, NR'', NHCOR'' or CF₃, where R'' is a linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, a linear, cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl,
 10 trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear
 15 or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3,
 20 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched
 25 chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

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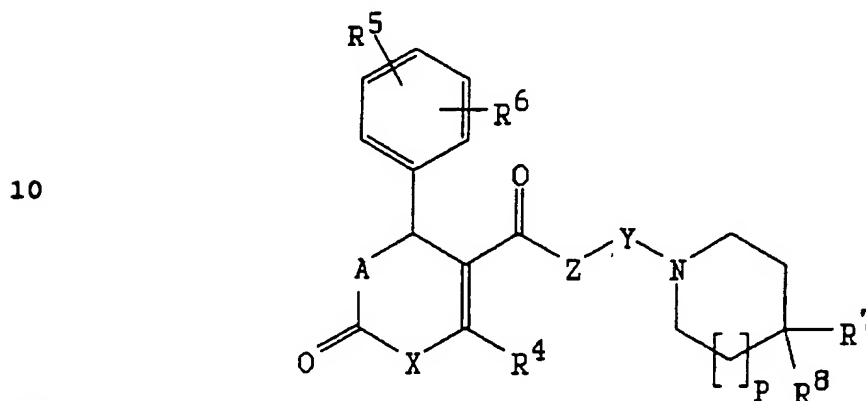


35 wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR₂^{iv}, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv},

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where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

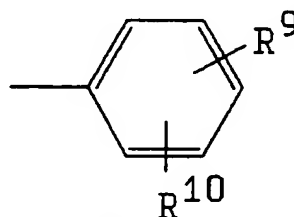
11. A compound having the structure:



wherein A and X are independently the same or different and are CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R^4 is H, a linear, cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1,

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2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , N_3 or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , COSH, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



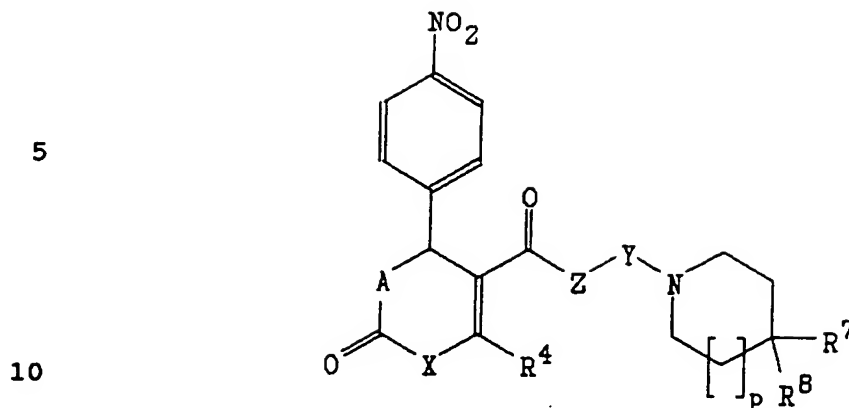
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

12. The compound of claim 11, wherein the compound has

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the structure:



wherein A and X are independently the same or different and are CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein Y is -

15 $(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' ,

20 NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R^4 is H, a linear, cyclic or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl

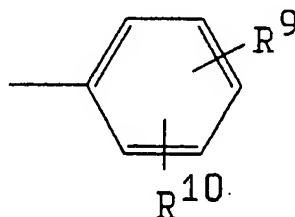
25 or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl

30 group, where W^0 is O , S or NH , where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and

35 R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR_2' , NHCOR' , CONH_2 , CONHR' , CONR_2' , COOH , COOR' , CHO , COR' , COSH , COSR' ,

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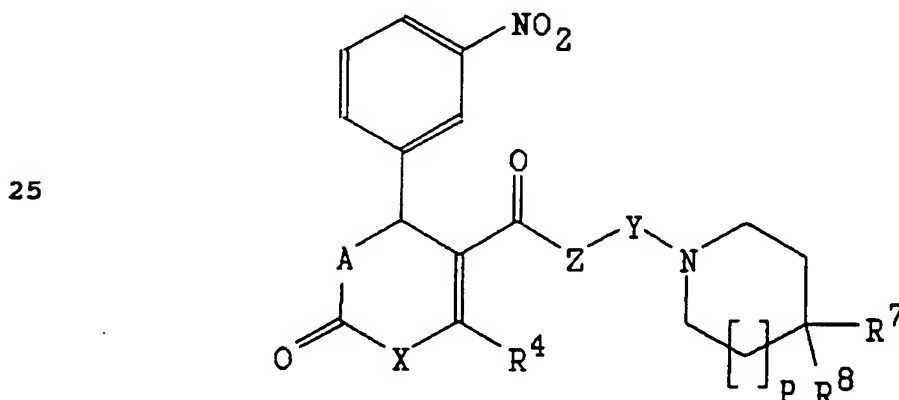
COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:



10

wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

13. The compound of claim 11, wherein the compound has the structure:



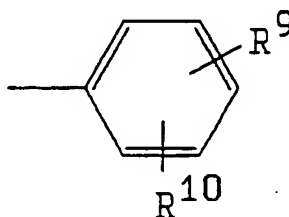
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wherein A and X are independently the same or different and are CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and

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are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein R⁴ is H, or a linear or branched chain, or cyclic alkyl group; and wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

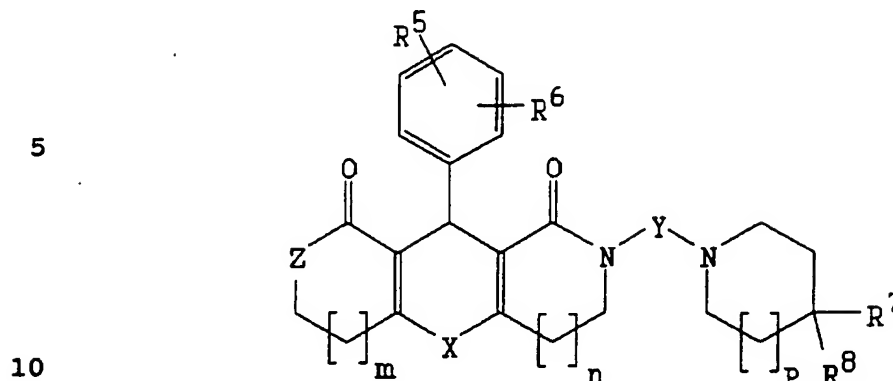
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20 wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

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14. A compound having the structure:



wherein X is CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein Y is -(CH₂)_h-, where h is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein m and n are independently the same or different and are 0 or 1; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, N₃ or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfone, or mono- or dialkylamino group, or together constitute a methylenedioxy group; and wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

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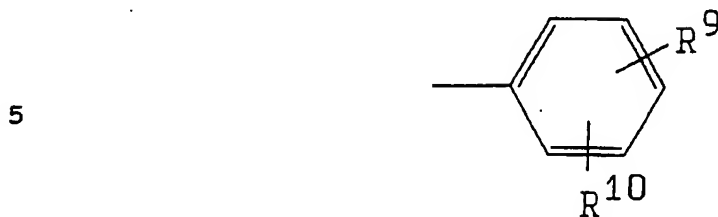
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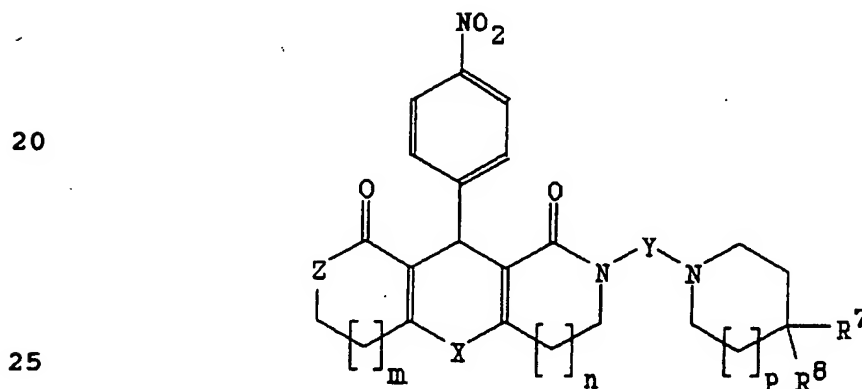
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group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , $\text{NR}^{\text{iv}2}$, NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

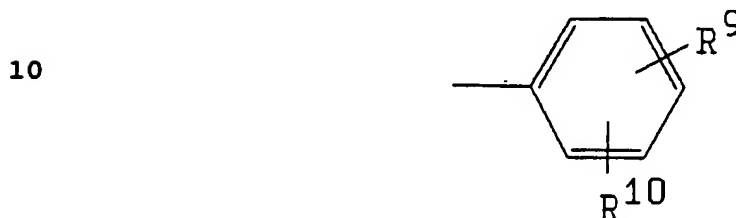
15 15. The compound of claim 14, wherein the compound has the structure:



wherein X is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein Y is $-(\text{CH}_2)_h-$, where h is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein j is 1 or 2; wherein p is 0, 1 or 2; wherein m and n are independently the same or different and are 0 or 1; and wherein R^7 and R^8 are independently the same or

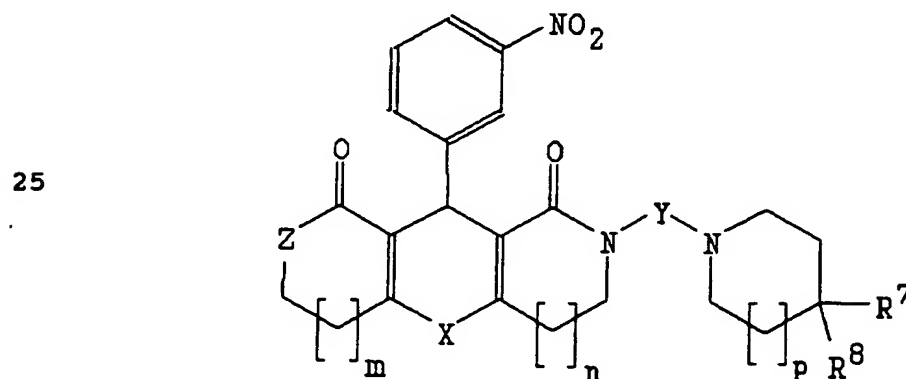
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different and are H, CN, CF₃, OH, OR''', OCOR''', NH₂, NHR''', NR'''₂, or NHCOR''', where R''' is a linear chain alkyl group, a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, F, OH, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R^{iv} is a linear or branched chain alkyl group.

16. The compound of claim 14, wherein the compound has the structure:

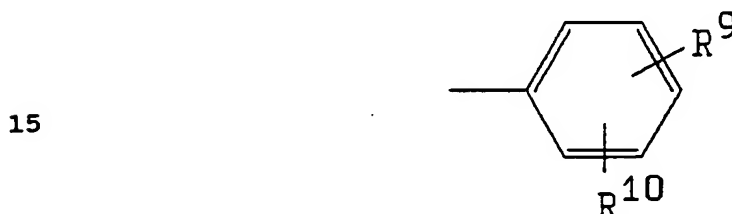


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wherein X is CH₂, CR₂, NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein Y is -(CH₂)_h-, where h is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k- where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR',

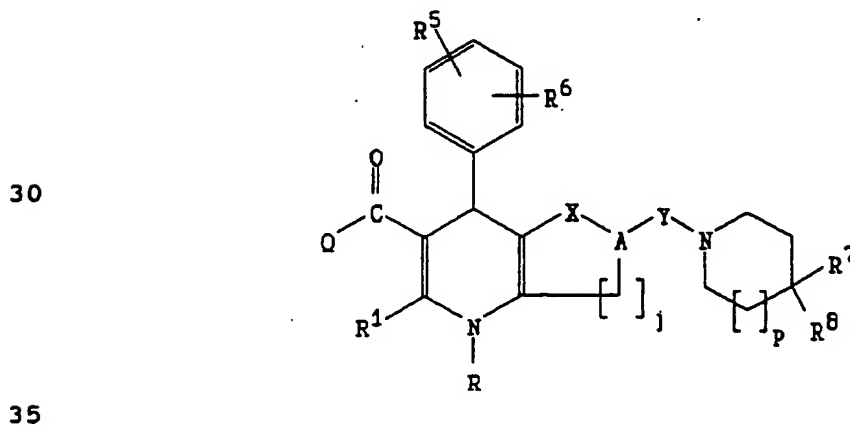
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NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein m, n, and p are independently the same or different and are 0 or 1; and wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃,
 5 OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,
 10 quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv},
 20 OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

25 17. A compound having the structure:



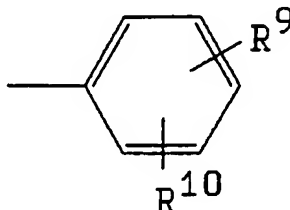
wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR''₂, NR''OH, NR''OR'' or a linear or branched chain alkyl

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group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 , or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein X is C=O, CH_2 , CR^5_2 , NH, NR^6 , $NCHO$, $NCOR^6$, NOH , O or S, where R' is a methyl, ethyl or propyl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , N_3 or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfone, or mono- or dialkyl-amino group, or together constitute a methylenedioxy group; wherein A is CH; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein j is 1 or 2; wherein p is 0, 1 or 2; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl

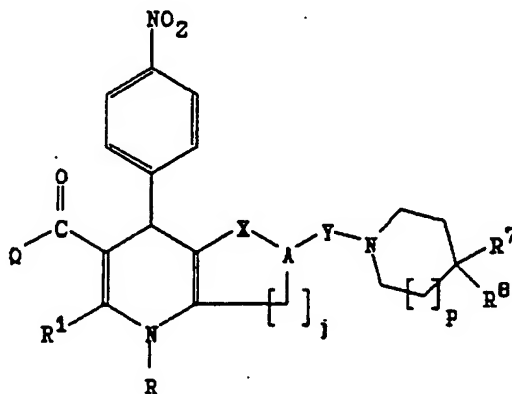
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group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

18. The compound of claim 17, wherein the compound has the structure:



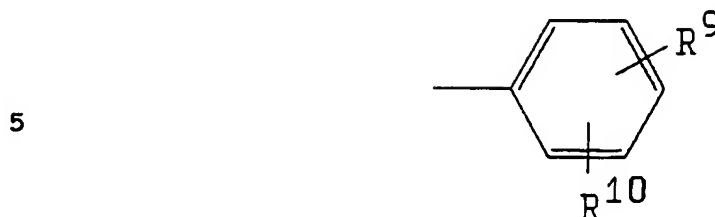
wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$ or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or

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an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_tW$, where W is NH_2 ,
 5 NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 , or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1
 10 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein X is C=O, CH_2 , CR^a_2 , NH, NR^a , $NCHO$, $NCOR^a$,
 15 NOH , O or S, where R^a is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group; wherein A is CH; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4;
 20 $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein j is 1 or 2; wherein p is 0, 1 or 2; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 ,
 25 $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,
 30 furyl or thiophene group, or an aryl group having the

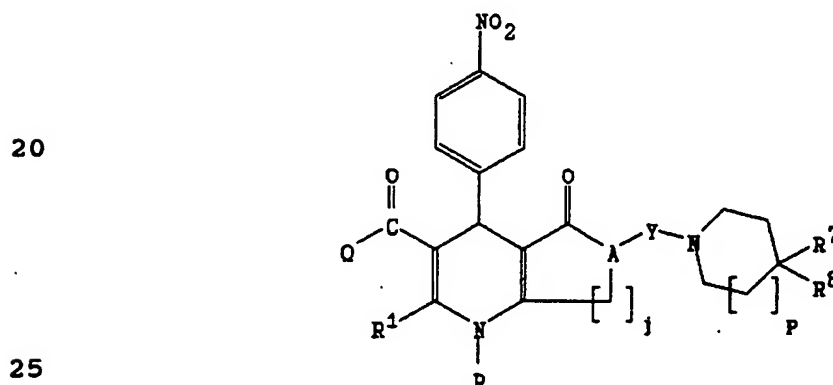
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structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

15 19. The compound of claim 18, wherein the compound has the structure:



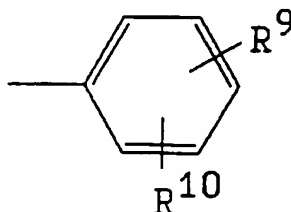
wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$ or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(\text{CH}_2)_q\text{W}$, where W is NH_2 ,

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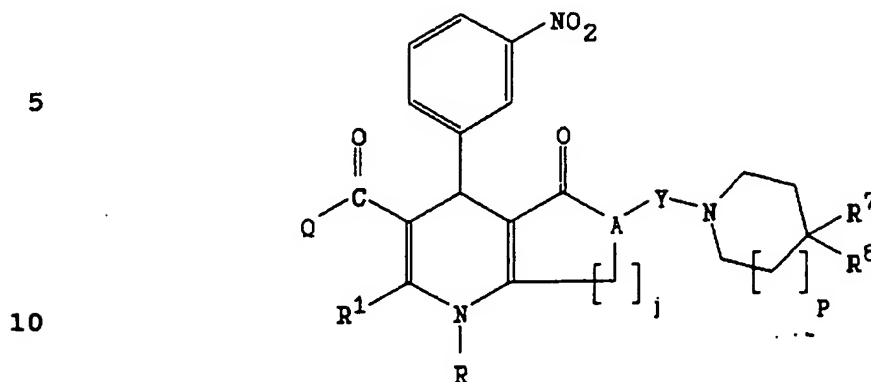
NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 , or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$,
 or a linear or branched chain alkyl group, or an
 arylalkyl group, or an alkenyl or alkynyl group, or an
 aryl group, where R' is a linear or branched chain alkyl
 5 group, or an aryl group, where W^0 is O, S or NH, where W^1
 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and
 where R' is a linear or branched chain alkyl group, or an
 aryl group, where Z^- is a pharmaceutically acceptable
 counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4,
 10 5 or 6; wherein A is CH; wherein Y is $-(\text{CH}_2)_n-$, where n is
 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h\text{-O-}(\text{CH}_2)_k-$, where h and k are
 independently the same or different and are 2, 3 or 4;
 $-(\text{CH}_2)_h\text{-CH=CH-}(\text{CH}_2)_k$
 $-$; or $-(\text{CH}_2)_h\text{-C}\equiv\text{C-}(\text{CH}_2)_k-$, where h and k are independently
 15 the same or different and are 1, 2, 3 or 4; wherein j is
 1 or 2; wherein p is 0, 1 or 2; and wherein R^7 and R^8 are
 independently the same or different and are H, CN, CF_3 ,
 OH, OR' , OCOR' , NH_2 , NHR' , NR_2' , NHCOR' , CONH_2 , CONHR' ,
 CONR_2' , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$
 20 or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched
 chain alkyl or cycloalkyl group, or are a heteroaryl
 group comprising a pyridyl, indolyl, indolylalkyl,
 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 group, or an aryl group having the structure:



30 wherein R^9 and R^{10} are independently the same or different
 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} ,
 $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 where R' is a linear or branched chain alkyl group, and
 35 R^{iv} is a linear or branched chain alkyl group, and q is 2,
 3, 4 or 5.

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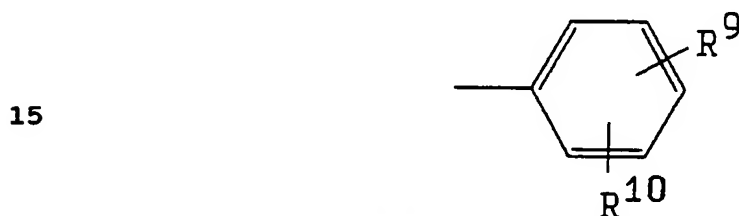
20. The compound of claim 18, wherein the compound has the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein A is CH; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and

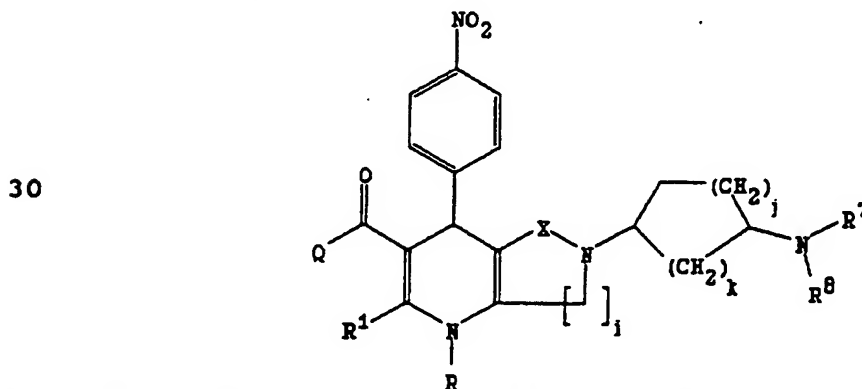
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k are independently the same or different and are 1, 2, 3 or 4; wherein j is 1 or 2; wherein p is 0, 1 or 2; and wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5.

25 21. A compound having the structure:



35 wherein X is $C=O$, CH_2 , CR^2_2 , NH, NR^2 , $NCHO$, $NCOR^2$, NOH , O or S, where R^2 is a methyl, ethyl or propyl group; wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR'_2''' , $NR''OH$,

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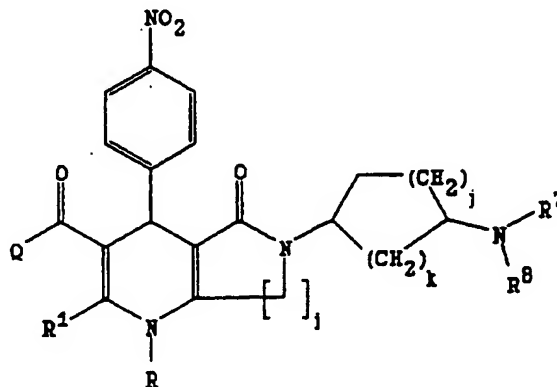
NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein i is 1 or 2; and wherein j and k are independently the same or different and are 0, 1, 2 or 3.

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22. The compound of claim 21, wherein the compound has the structure:

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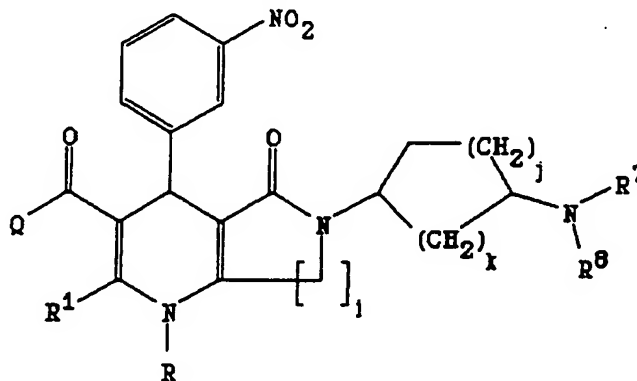
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wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein i is 1 or 2; and wherein j and k are independently the same or different and are 0, 1, 2 or 3.

23. A compound having the structure:



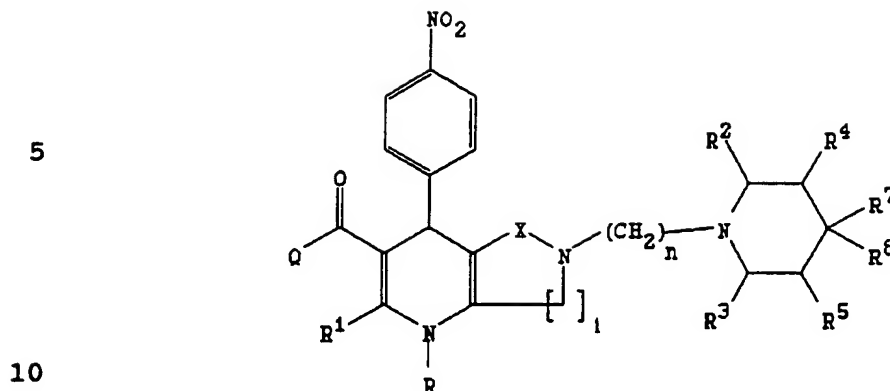
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wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein i is 1 or 2; and wherein j and k are independently the same or different and are 0, 1, 2 or 3.

24. The compound of claim 18, wherein the compound has

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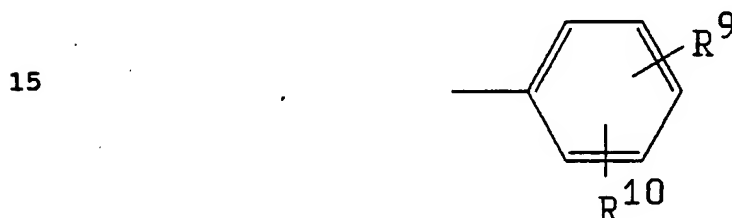
the structure:



wherein X is C=O, CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R² and R³ are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein R⁴ and R⁵ are independently the same or different

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and are a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different
 5 and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl,
 10 indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

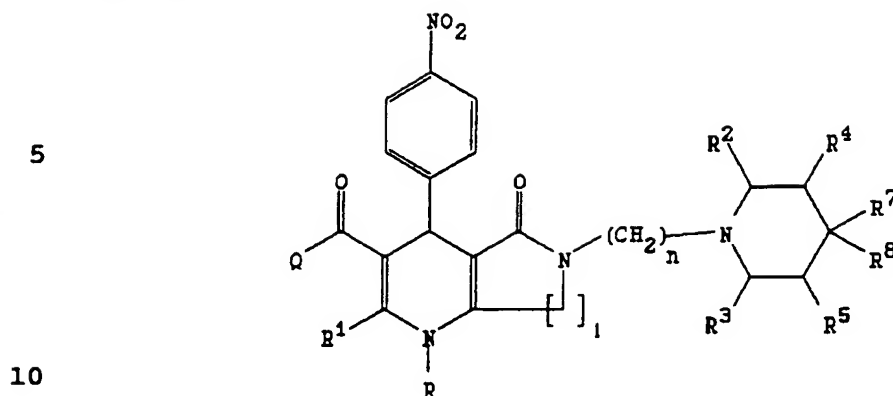


wherein R^9 and R^{10} are independently the same or different
 20 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein i is 1 or 2; and wherein n is 2, 3 or
 25 4.

25. The compound of claim 24, wherein the compound has

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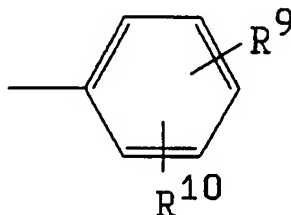
the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R² and R³ are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein R⁴ and R⁵ are independently the same or different and are a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a

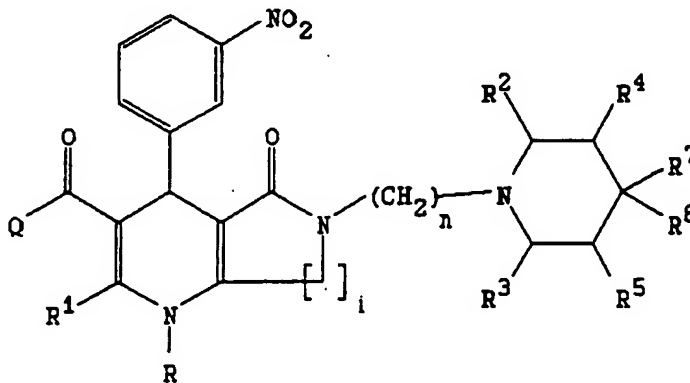
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hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR', OCOR', NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, 5 $CONR'_2$, COOH, COOR', CHO, COR', COSH, COSR', $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene 10 group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv},
20 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein i is 1 or 2; and wherein n is 2, 3 or 4.

25 26. The compound of claim 20, wherein the compound has
the structure:



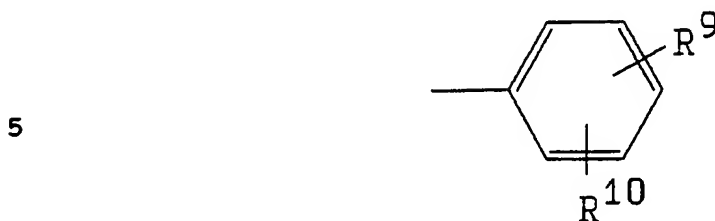
wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'',

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$\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$ or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group; or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 and R^3 are independently the same or different and are a linear or branched chain alkyl group, or an aryl group; wherein R^4 and R^5 are independently the same or different and are a linear or branched chain alkyl, alkoxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR_2' , NHCOR' , CONH_2 , CONHR' , CONR_2' , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

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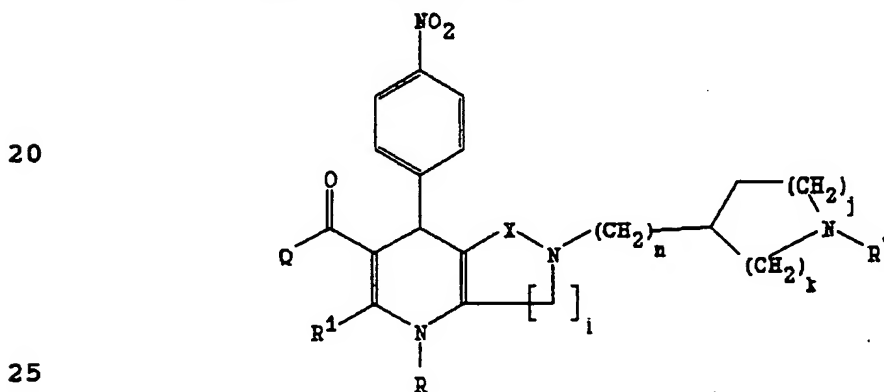
group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv_2} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein i is 1 or 2; and wherein n is 2, 3 or 4.

15

27. A compound having the structure:



wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$ or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl,

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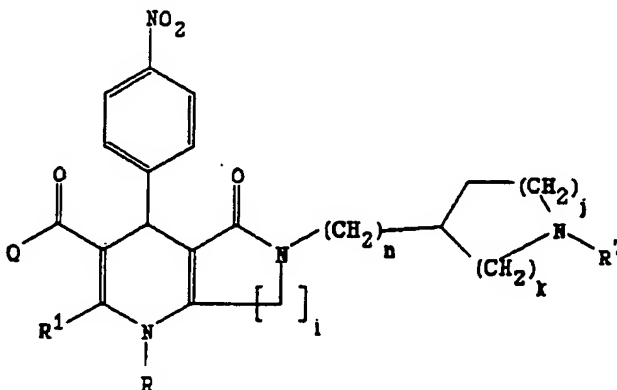
hydroxyalkyl or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 is an aryl or diarylalkyl group; wherein i is 1 or 2; wherein n is 2, 3 or 4; and wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4.

15

28. The compound of claim 27, wherein the compound has the structure:

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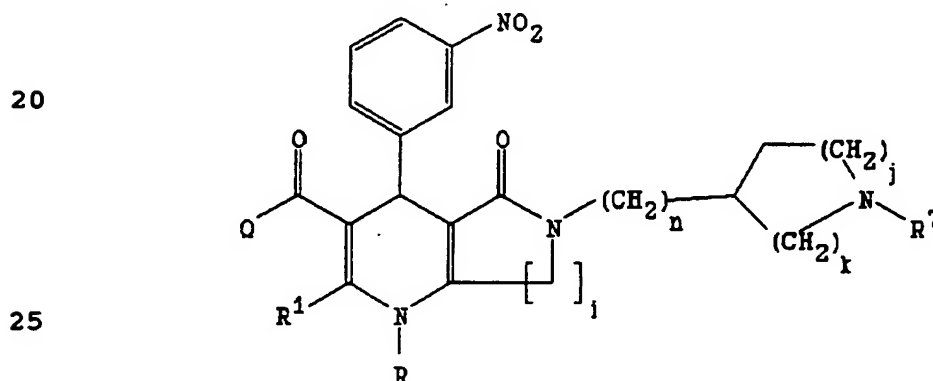


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$ or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl,

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azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 is an aryl or diarylalkyl group; wherein i is 1 or 2; wherein n is 2, 3 or 4; and wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4.

29. A compound having the structure:



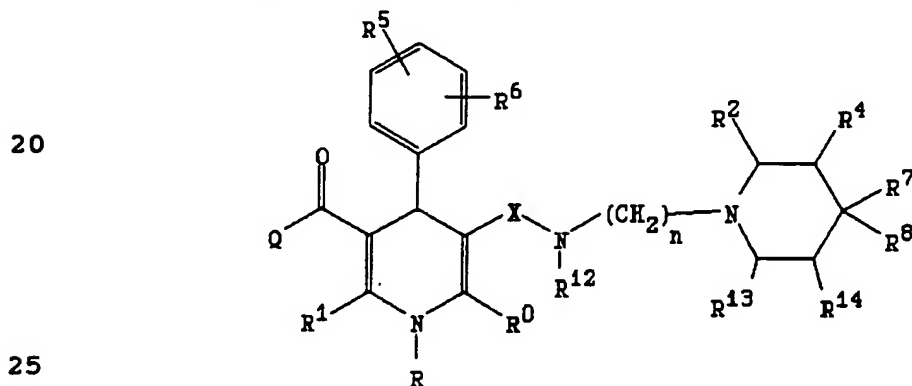
wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl,

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hydroxyalkyl or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 is an aryl or diarylalkyl group; wherein i is 1 or 2; wherein n is 2, 3 or 4; and wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4.

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30. A compound having the structure:



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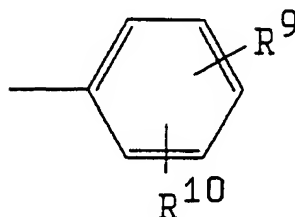
wherein X is $C=O$, CH_2 , CR^a_2 , NH , NR^a , $NCHO$, $NCOR^a$, NOH , O or S, where R^a is a methyl, ethyl or propyl group; wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$ or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different

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and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR'_2 , NHOH , $\text{N}^+\text{R}'_3\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , NHOH , $\text{N}^+\text{R}'_3\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^{13} , and R^{14} are independently the same or different and are H, or a linear or branched chain alkyl, hydroxyalkyl, alkoxyalkyl, amino alkyl, or aryl group; wherein R^4 is a linear or branched chain alkyl, alkoxyalkyl, hydroxyalkyl, or a linear or branched chain alkenylalkyl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , N_3 , CF_3 , a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or

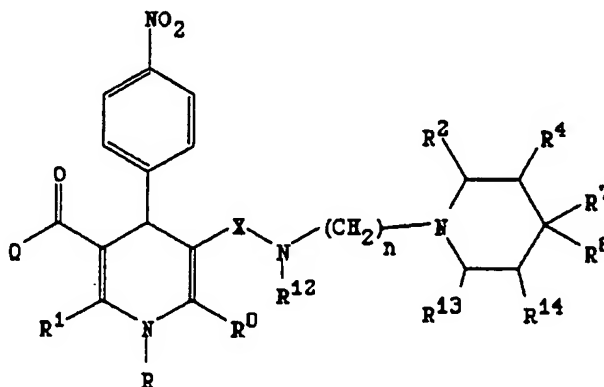
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thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv_2} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

31. The compound of claim 30 having the structure:

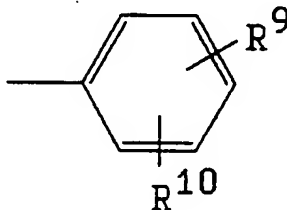


wherein X is $\text{C}=\text{O}$, CH_2 , CR^a_2 , NH , NR^a , NCHO , NCOR^a , NOH , O or S , where R^a is a methyl, ethyl or propyl group; wherein Q is OH , OR'' , SH , SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different

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and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^{13} , and R^{14} are independently the same or different and are H, or a linear or branched chain alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, or aryl group; wherein R^4 is a linear or branched chain alkyl, alkoxyalkyl, hydroxyalkyl, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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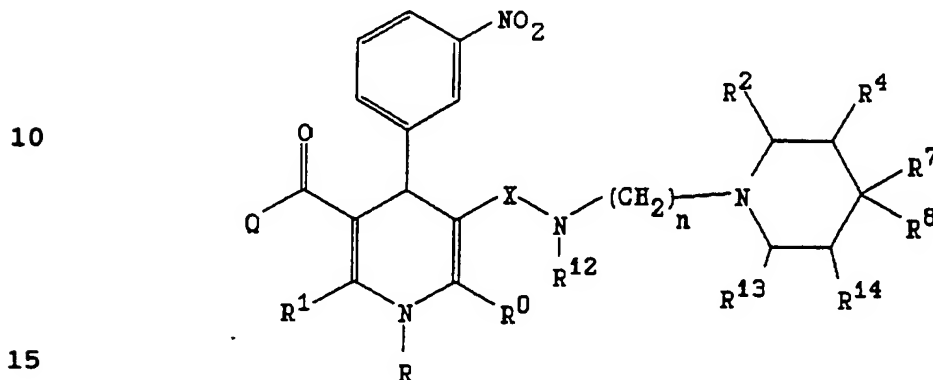
35 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$,

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where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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32. The compound of claim 30 having the structure:



wherein X is $C=O$, CH_2 , CR^a_2 , NH , NR^a , $NCHO$, $NCOR^a$, NOH , O or S , where R^a is a methyl, ethyl or propyl group; wherein Q is OH , OR'' , SH , SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxy-alkyl, or an aryl group, or $(CH_2)_xW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_yW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O , S or NH , where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a

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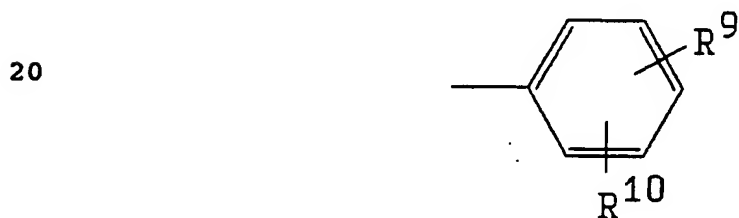
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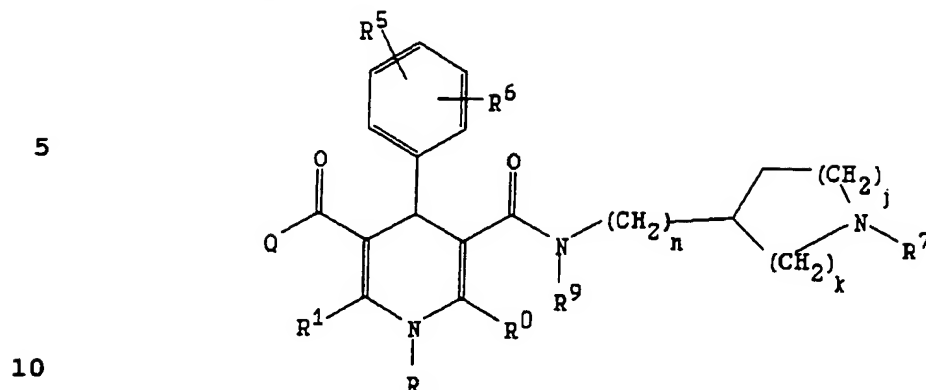
linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 , R^{13} , and R^{14} are independently the same or different and are H, or a linear or branched chain alkyl, hydroxyalkyl, alkoxyalkyl, amino alkyl or aryl group; wherein R^4 is a linear or branched chain alkyl, alkoxyalkyl, hydroxyalkyl, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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33. A compound having the structure:

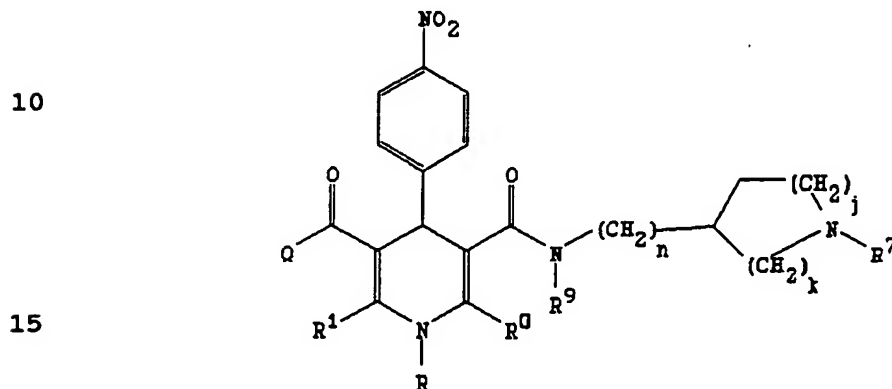


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, N₃, CF₃, a linear or branched chain alkyl, alkoxy, alkoxy-carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono-

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or dialkylamino group, or together constitute a methylenedioxy group; wherein R^7 is an aryl or diarylalkyl group; wherein R^9 is H or a linear chain alkyl group; wherein j and k are independently the same or different
 5 and are 0, 1, 2 or 3; and wherein n is 2, 3 or 4.

34. The compound of claim 33 having the structure:

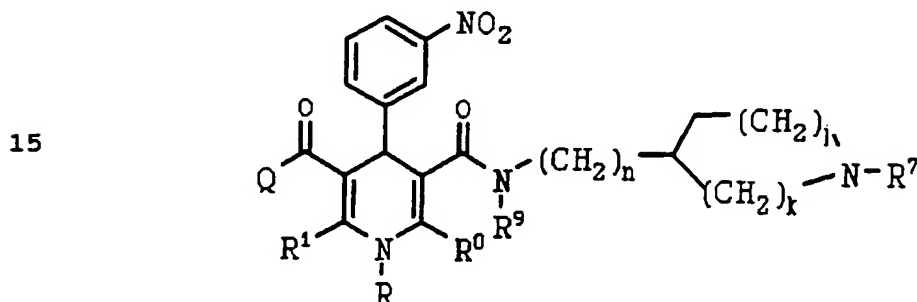


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R
 25 is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl,
 30 hydroxyalkyl, or an aryl group, or (CH₂)_lW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_lW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl
 35 group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an

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aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R' is an aryl or diarylalkyl group; wherein R⁹ is a H or linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2 or 3; and wherein n is 2, 3 or 4.

10 35. The compound of claim 33 having the structure:



20 wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, 25 cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain 30 alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an 35 arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl

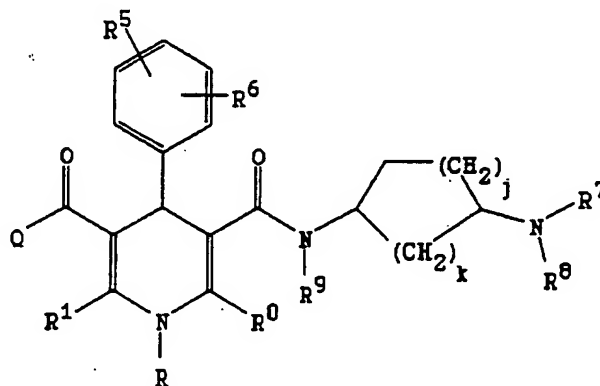
-599-

group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 is an aryl or diarylalkyl group; wherein R^9 is H or a linear chain alkyl group; and wherein j and k are independently the same or different and are 0, 1, 2 or 3.

36. A compound having the structure:

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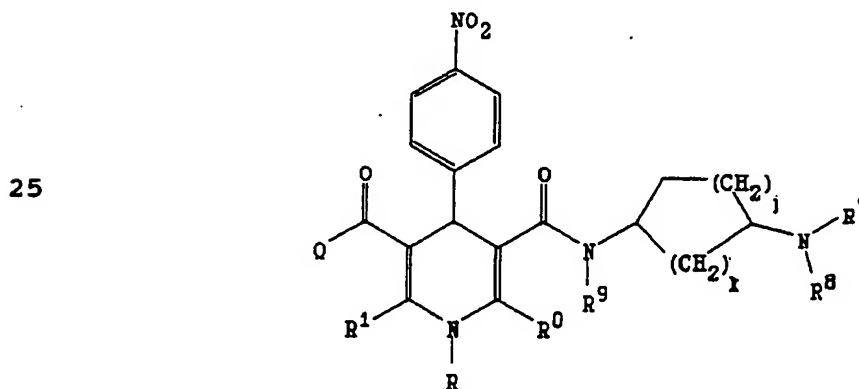


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 ,

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NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, N₃, CF₃, a linear or branched chain alkyl, alkoxy, alkoxy-carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R⁷ is an aryl or diarylalkyl group; wherein R⁹ is a linear chain alkyl group; and wherein j and k are independently the same or different and are 0, 1, 2 or 3.

37. The compound of claim 36 having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or

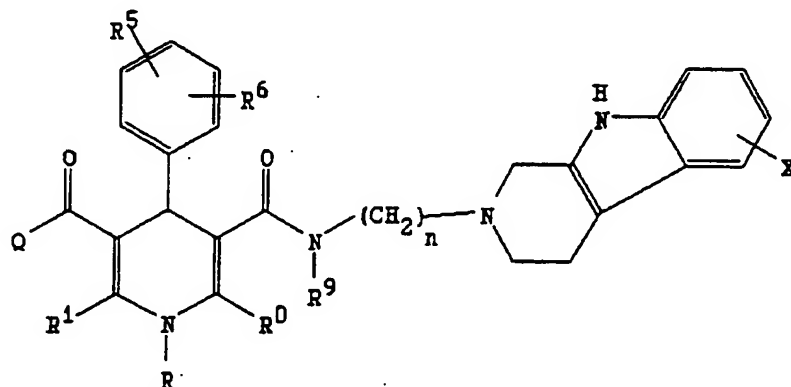
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an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^9 is a linear chain alkyl group; and wherein j and k are independently the same or different and are 0, 1, 2 or 3.

38. A compound having the structure:

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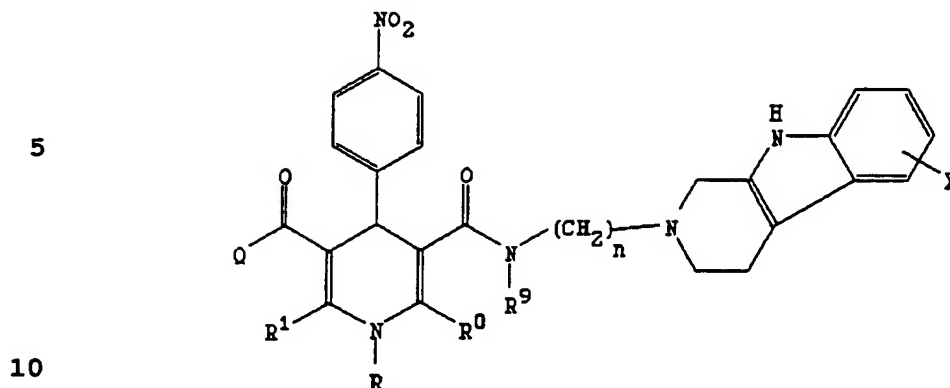
wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR'''OH$, $NR'''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the

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same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein X is H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, or a linear or branched chain alkyl, alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, or hydroxylalkyl group, or an aryl group; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , N_3 , CN, NH_2 , or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^9 is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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39. The compound of claim 38 having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein X is H, OH, Cl, Br, I, F, NO₂, CN, NH₂, or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R is H or a linear

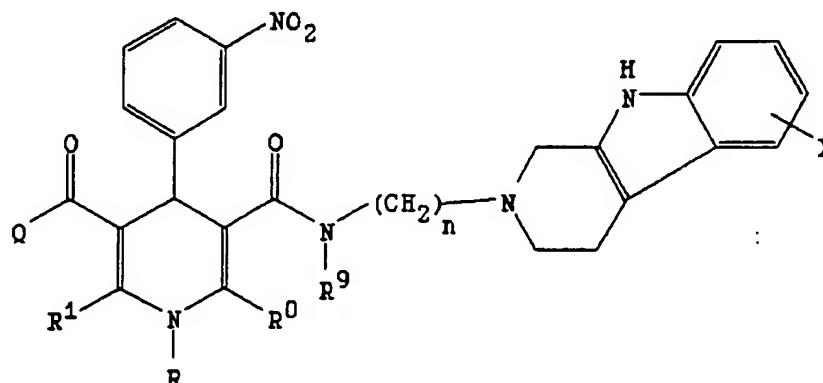
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or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, or a linear or branched chain alkyl, alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxy-
 5 alkyl, trihaloalkoxyalkyl, aminoalkyl, or hydroxylalkyl group, or an aryl group; wherein R^9 is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

40. The compound of claim 38 having the structure:

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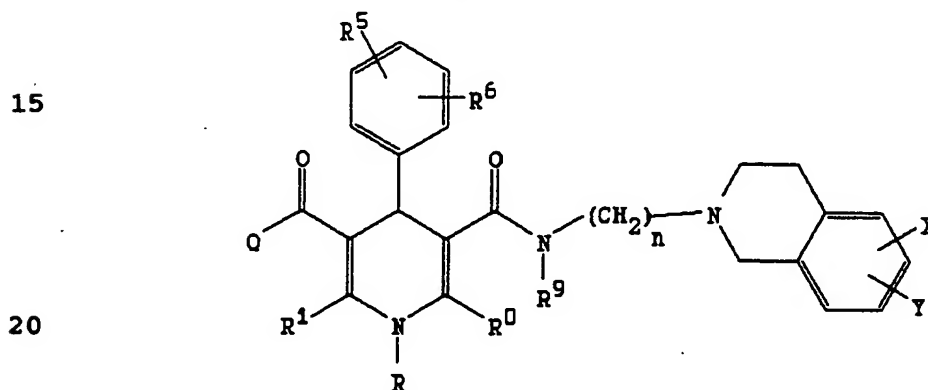


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' ,
 20 $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or
 25 branched chain alkyl group, or an aryl group; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein X is H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or
 30 mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-
 35 alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_4W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_4W^1$, or a

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linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^9 is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

41. A compound having the structure:

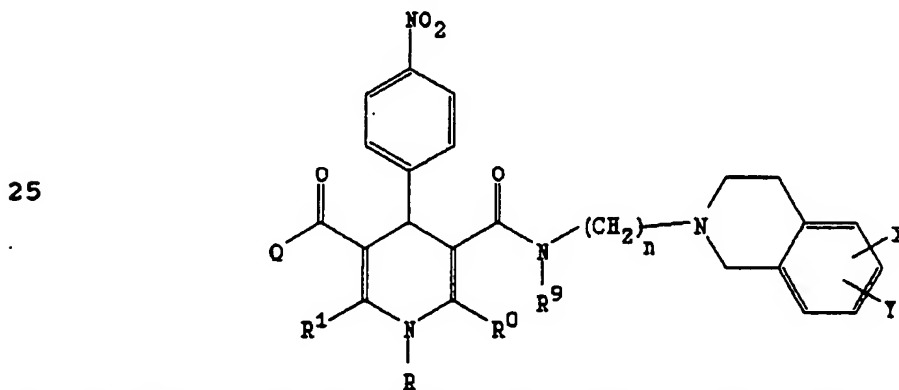


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein X and Y are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl,

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aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^5 and R^6 are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , N_3 , CN, NH_2 , or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R^9 is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

42. The compound of claim 41 having the structure:



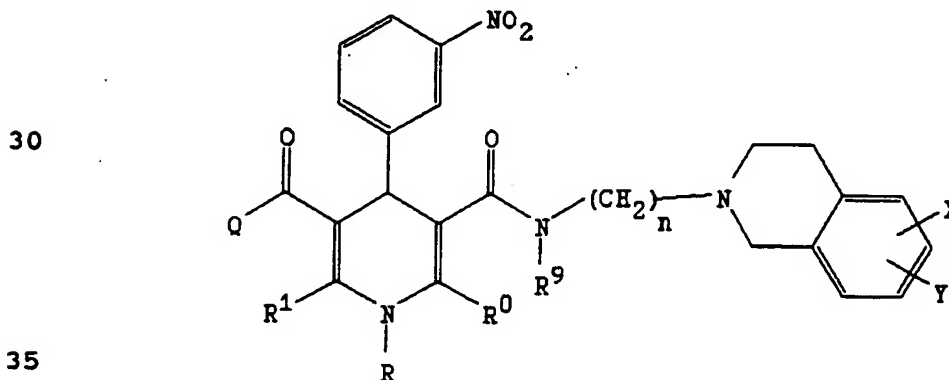
30 wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein X and Y are independently the same or different and are H,

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OH, Cl, Br, I, F, NO₂, CN, NH₂, or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein X and Y are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, NH₂, or CF₃, or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R⁹ is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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43. The compound of claim 41 having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'',

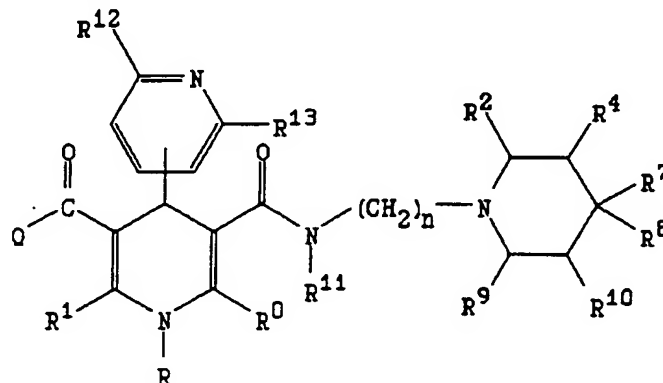
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$\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein X and Y are independently the same or different and are H, OH, Cl, Br, I, F, NO_2 , CN, NH_2 , or CF_3 , or a linear or branched chain alkyl, alkoxy, alkoxycarbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^9 is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

44. A compound having the structure:

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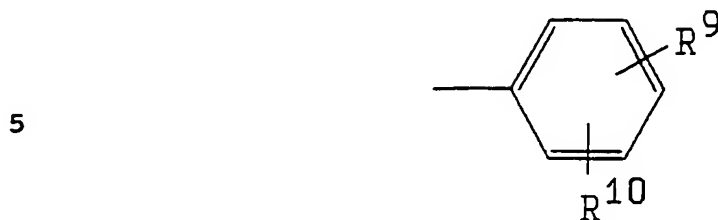


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wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is a H or linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

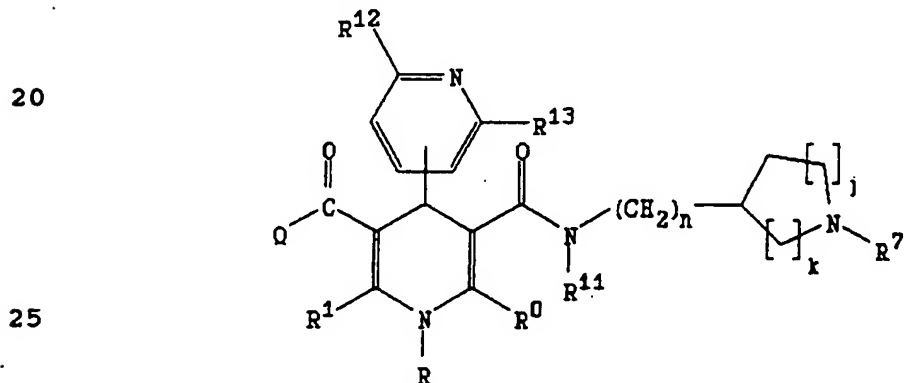
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group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 10 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and
 15 wherein n is 2, 3 or 4.

45. A compound having the structure:

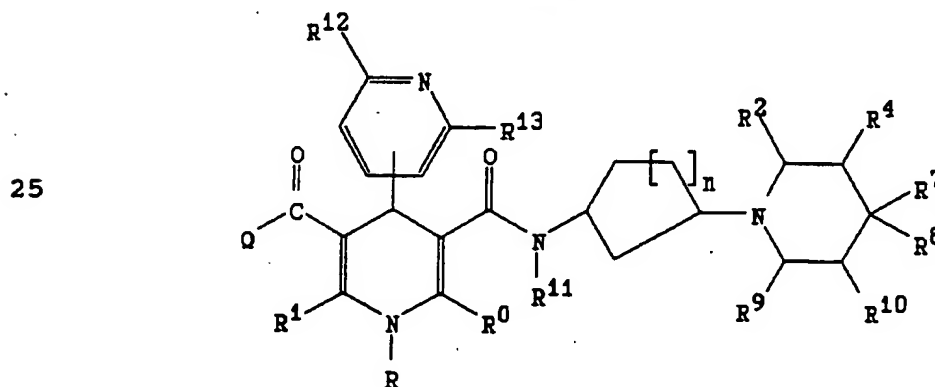


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl
 30 group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R
 35 is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain

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alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$,
 5 or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and
 10 where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 is an aryl or diarylalkyl group; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12}
 15 and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

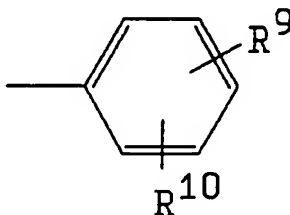
20 46. A compound having the structure:



30 wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or
 35 branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R

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is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

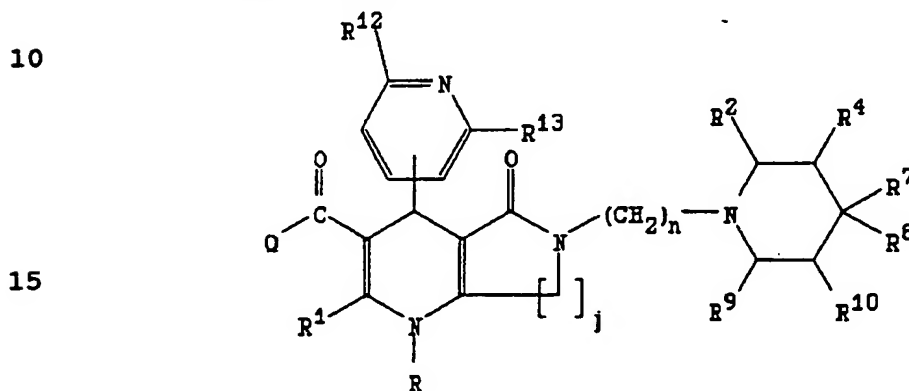


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$,

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$\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 where R' is a linear or branched chain alkyl group, and
 R^{iv} is a linear or branched chain alkyl group, and q is 2,
 3, 4 or 5; wherein R^{12} and R^{13} are independently the same
 5 or different and are H or a linear chain alkyl group; and
 wherein n is 0, 1, 2, 3 or 4.

47. A compound having the structure:

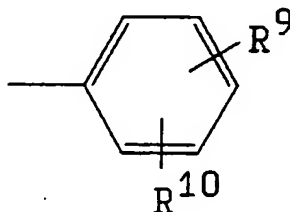


wherein Q is OH , OR'' , SH , SR''' , NH_2 , NHR'''' , NR_2''' ,
 20 $\text{NR}'''\text{OH}$, $\text{NR}'''\text{OR}'''$, or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl
 group, or an aryl group, where R'' is H, a linear or
 branched chain alkyl group, trialkylsilylalkyl,
 cyanoalkyl, or an aryl group, and R''' is a linear or
 25 branched chain alkyl group, or an aryl group; wherein R
 is H or a linear or branched chain alkyl or acyl group,
 or an aryl group; wherein R^1 is H, a linear or branched
 chain alkyl, an alkoxyalkyl, azidoalkyl,
 aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl,
 30 aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_j\text{W}$,
 where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2
 or $\text{CH}_2\text{W}^0(\text{CH}_2)_k\text{W}^1$, or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl
 group, or an aryl group, where R' is a linear or branched
 35 chain alkyl group, or an aryl group, where W^0 is O, S or
 NH , where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3
 or NO_2 , and where R' is a linear or branched chain alkyl

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group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 , R^9 and R^{10} are independently the same or different and are a linear or branched chain alkyl group; wherein R^4 is a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

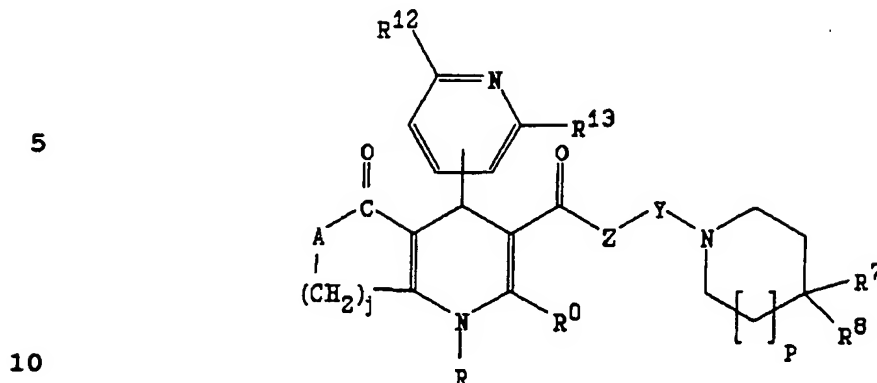
20



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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48. A compound having the structure:

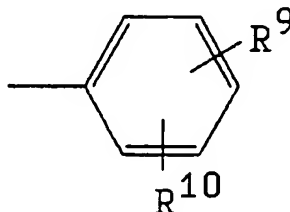


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH₂, CR₂, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Z is O, NH, NCHO, NCOR', NR', NOR', or CH₂, where R' is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and

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where R' is a linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ and R⁸ are independently the same or
 5 different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl,
 10 indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

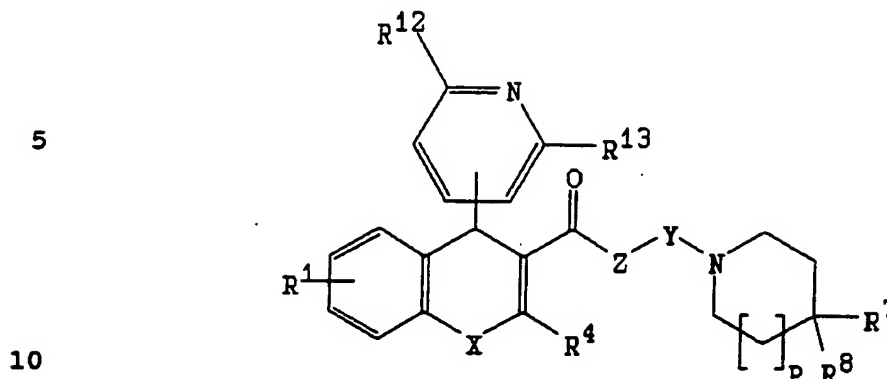
15



wherein R⁹ and R¹⁰ are independently the same or different
 20 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² and R¹³ are independently the same
 25 or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

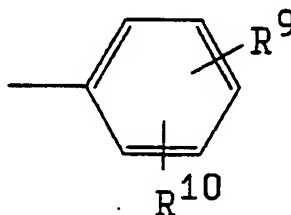
-617-

49. A compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^1 is H, Cl, Br, I, F, NO_2 , CN, OH, OR^2 , $OCOR^2$, NH_2 , NR^2 , $NHCOR^2$, or CF_3 , where R^2 is a linear or branched chain alkyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, COOH, $COOR'$, CHO, COR' , COSH, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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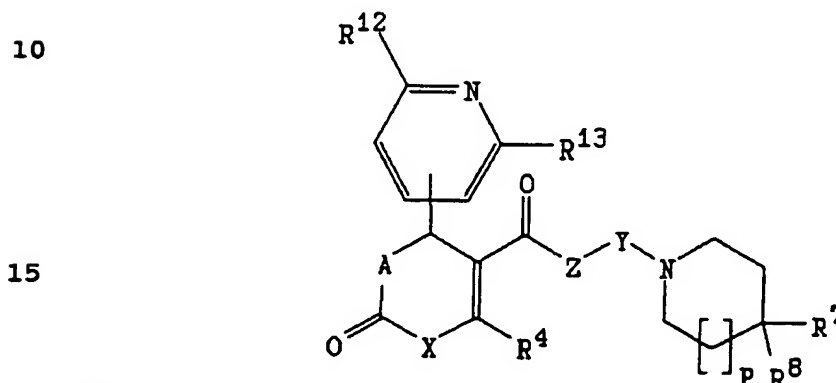
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$,

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$\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 where R' is a linear or branched chain alkyl group, and
 R^{iv} is a linear or branched chain alkyl group, and q is 2,
 3, 4 or 5; wherein R^{12} and R^{13} are independently the same
 5 or different and are H or a linear chain alkyl group; and
 wherein p is 0, 1, 2 or 3.

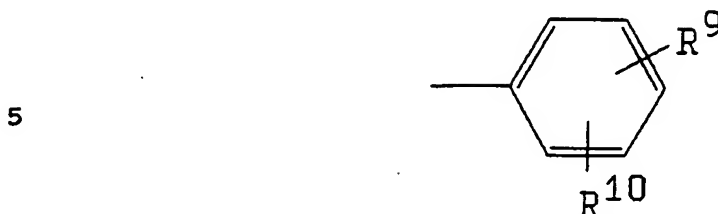
50. A compound having the structure:



wherein A is CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S,
 where R is a methyl, ethyl or propyl group; wherein Y is
 20 $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$,
 where h and k are independently the same or different and
 are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$,
 where h and k are independently the same or different and
 are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR',
 25 NOR' or CH_2 , where R' is a methyl, ethyl or propyl group;
 wherein X is NH, NR'', O or S, where R'' is H or a linear
 or branched chain alkyl or acyl group, or an aryl group;
 wherein R^4 is H, or a linear or branched chain alkyl
 group, or an aryl group; wherein R^7 and R^8 are independ-
 30 ently the same or different and are H, CN, CF_3 , OH, OR',
 OCOR', NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 ,
 COOH, COOR', CHO, COR', COSH, COSR', $\text{COO}(\text{CH}_2)_q\text{OH}$ or
 $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched
 chain alkyl or cycloalkyl group, or are a heteroaryl
 35 group comprising a pyridyl, indolyl, indolylalkyl,
 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

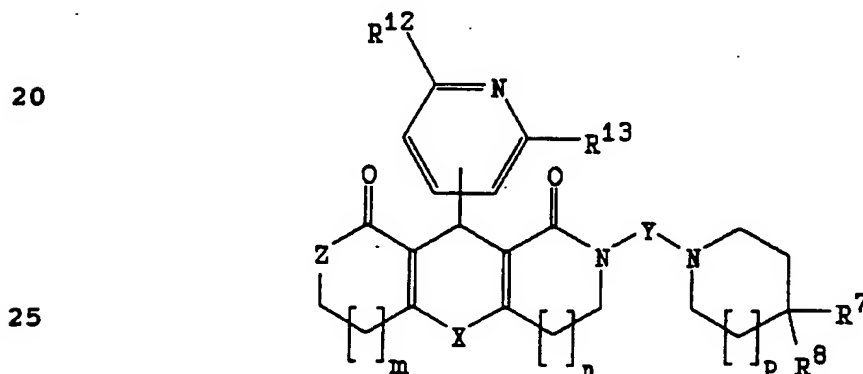
-619-

group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 10 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and
 15 wherein p is 0, 1, 2 or 3.

51. A compound having the structure:



wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein X is NH, NR' , O, or S, where R' is H or a linear or branched chain alkyl or acyl group,
 30 or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' ,

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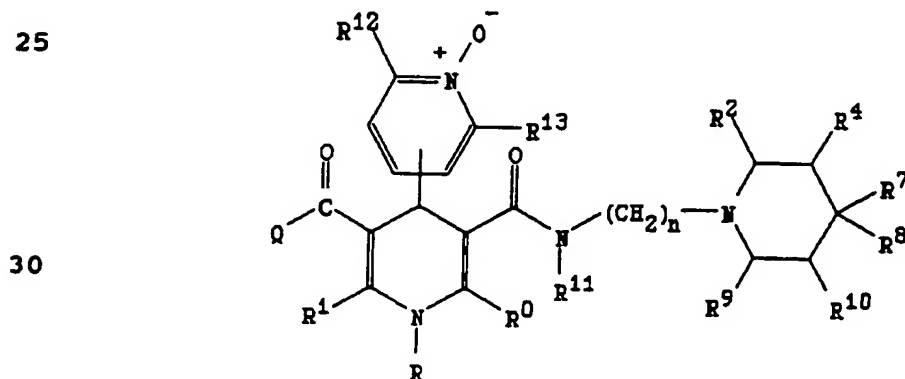
-620-

CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquin-
 5 olinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv},
 15 OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² and R¹³ are independently the same or different and are H or a linear chain alkyl group;
 20 wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

52. A compound having the structure:



wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR₂,
 35 NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or

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branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H or a linear or branched chain alkyl or acyl group,

5 or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂,

10 NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹

15 is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R², R⁹ and R¹⁰ are independently the same

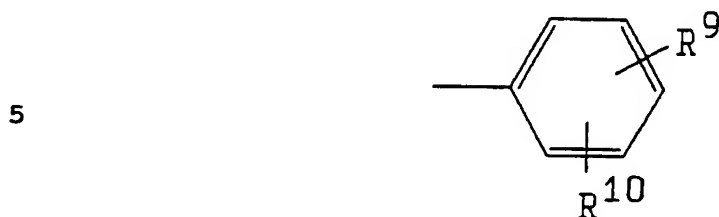
20 or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are

25 independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl

30 group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

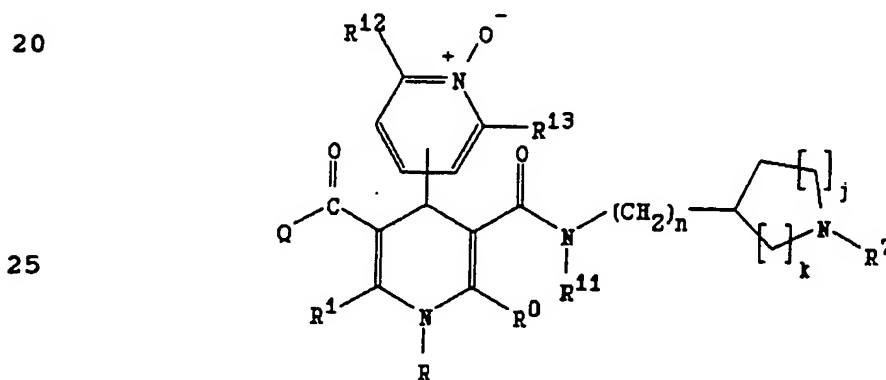
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group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

53. A compound having the structure:



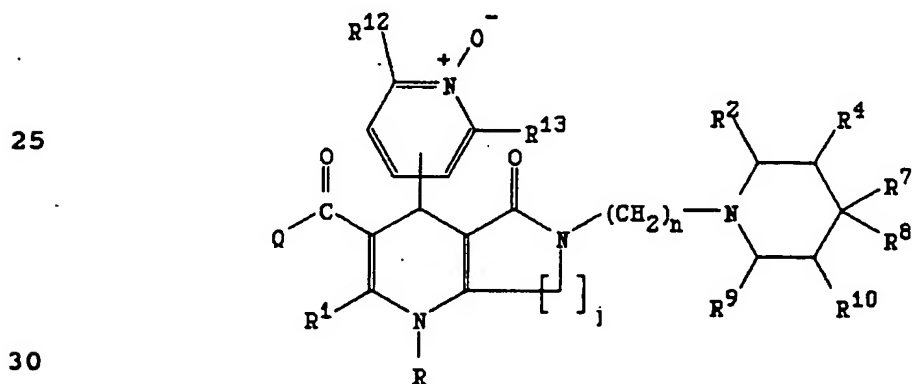
wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azido-

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alkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 is an aryl or diarylalkyl group; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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54. A compound having the structure:

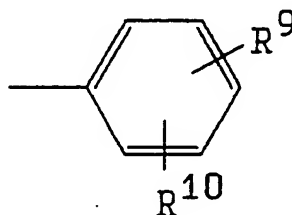


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or

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branched chain alkyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are a linear or branched chain alkyl group; wherein R^4 is a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$,

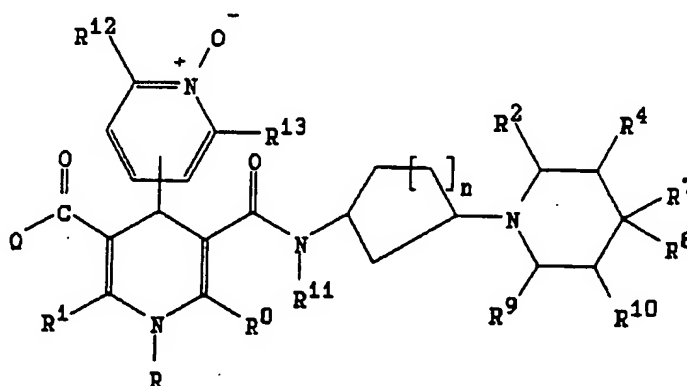
-625-

$\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2,
 3, 4 or 5; wherein R^{iv} is H or a linear chain alkyl group;
 5 wherein R^{12} and R^{13} are independently the same or different
 and are H or a linear chain alkyl group; wherein j is 1,
 2, 3 or 4; and wherein n is 2, 3 or 4.

55. A compound having the structure:

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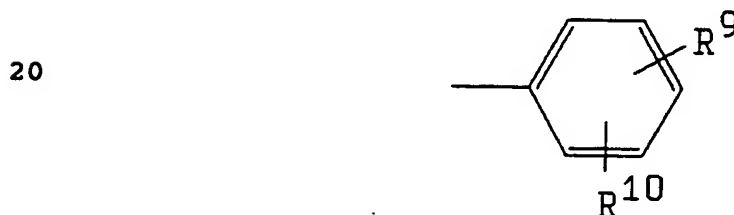
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20 wherein Q is OH , OR'' , SH , SR''' , NH_2 , NHR''' , NR_2''' ,
 $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl
 group, or an aryl group, where R'' is H, a linear or
 branched chain alkyl group, trialkylsilylalkyl,
 25 cyanoalkyl, or an aryl group, and R''' is a linear or
 branched chain alkyl group, or an aryl group; wherein R^0
 and R^1 are independently the same or different and are H,
 a linear or branched chain alkyl, an alkoxyalkyl, azido-
 alkyl, aminoalkoxyalkyl, azidoalkoxyalkyl,
 30 trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl
 group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$,
 NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched
 chain alkyl group, or an arylalkyl group, or an alkenyl
 or alkynyl group, or an aryl group, where R' is a linear
 35 or branched chain alkyl group, or an aryl group, where W^0
 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$,
 NHCOR' , N_3 or NO_2 , and where R' is a linear or branched

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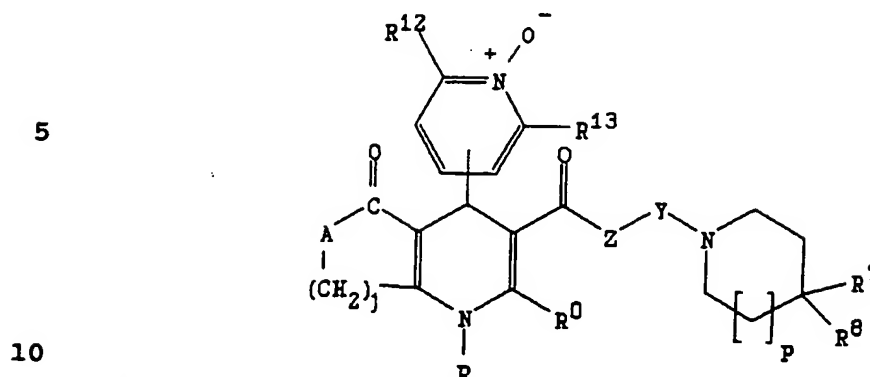
chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a
 5 linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different
 10 and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl,
 15 indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 25 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group;
 30 wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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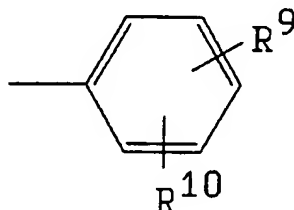
56. A compound having the structure:



wherein R^0 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH_2 , CR^a_2 , NH, NR^a , $NCHO$, $NCOR^a$, NOH , O or S, where R^a is a methyl, ethyl or propyl group; wherein Z is O, NH, $NCHO$, $NCOR'$, NR' , NOR' , or CH_2 , where R' is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched

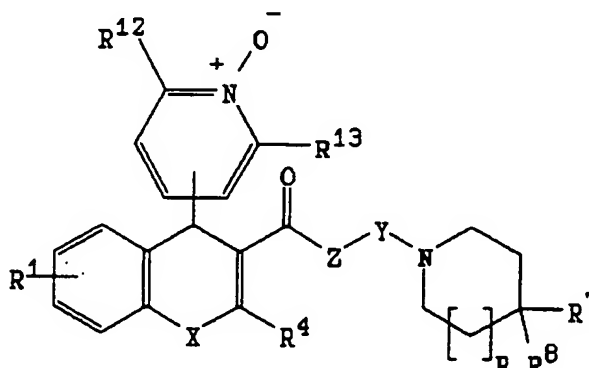
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chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

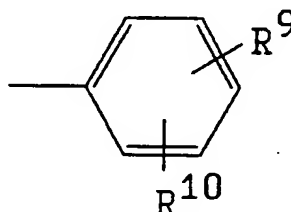
57. A compound having the structure:



wherein X is NH, NR'' , O, or S, where R'' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O,

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NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; or an aryl group; wherein R^1 is H, Cl, Br, I, F, NO_2 , CN, OH, OR^2 , OCOR^2 , NH_2 , NR^2 , NHCOR_2 , or CF_3 , where R^2 is a linear or branched chain alkyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



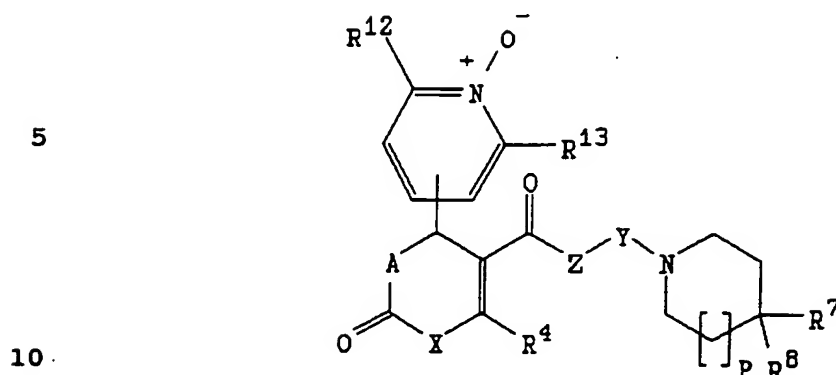
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

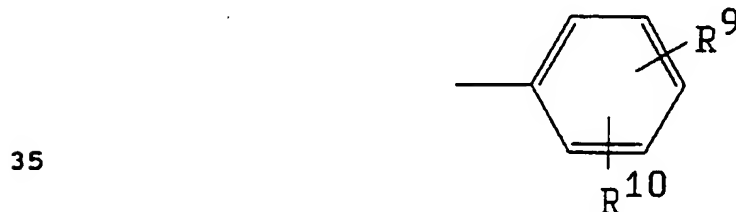
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58. A compound having the structure:



wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein X is NH , NR'' , O , or S , where R'' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different

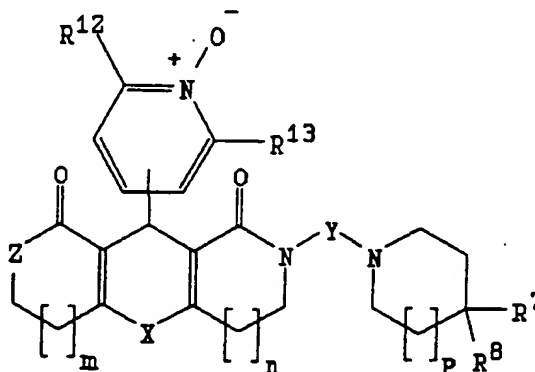
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and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2,
 5 3, 4 or 5; wherein R¹² and R¹³ are independently the same or different and are H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

59. A compound having the structure:

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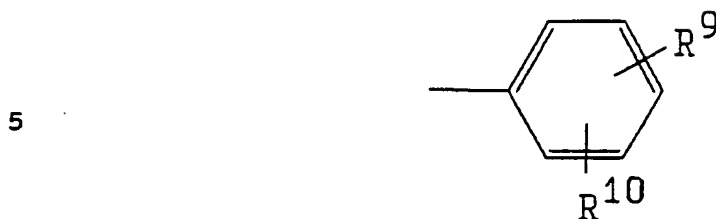
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wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-
 20 O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH₂, where R is a methyl, ethyl
 25 or propyl group; wherein X is NH, NR', O, or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR',
 30 CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl

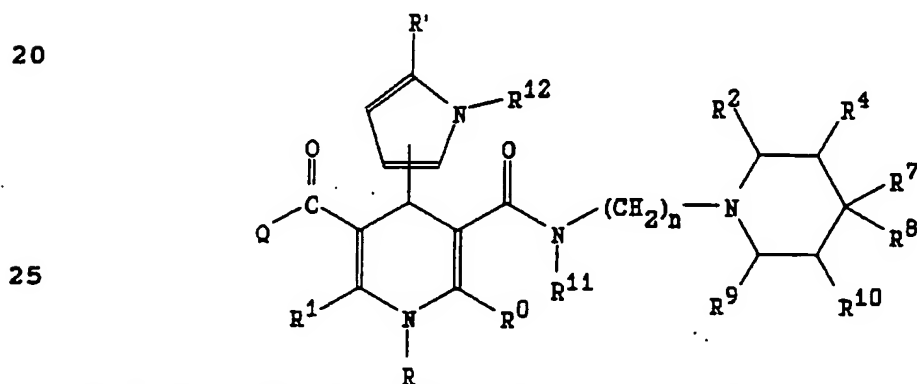
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group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv_2} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 10 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group;
 15 wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

60. A compound having the structure:

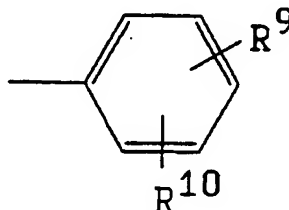


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl
 30 group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 ,
 35 R^1 and R' are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl,

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trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

30

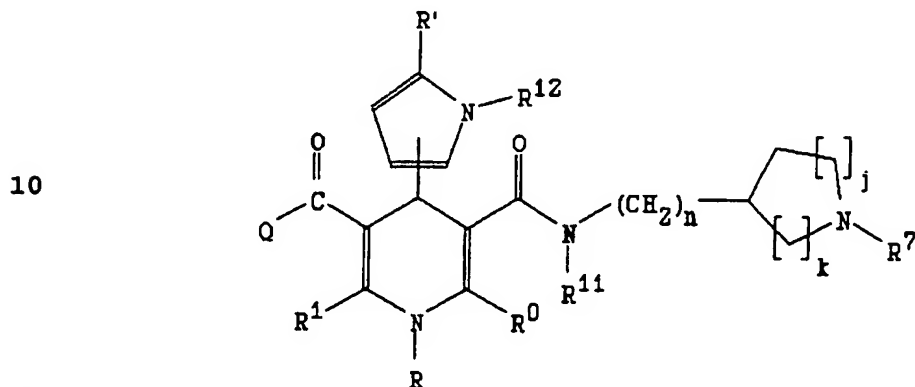


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR_2^{iv} , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2,

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3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; and wherein n is 2, 3 or 4.

5 61. A compound having the structure:

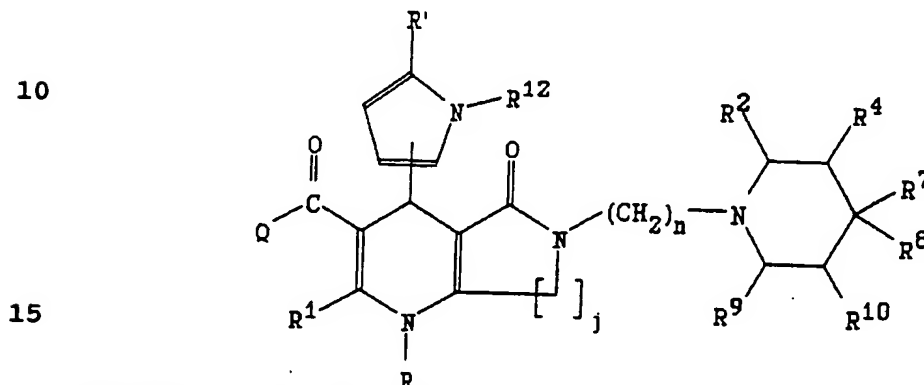


wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR₂', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰, R¹ and R' are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl

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group; wherein R^7 is an aryl or diarylalkyl group; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

62. A compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R¹ and R' are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R¹ and R' are

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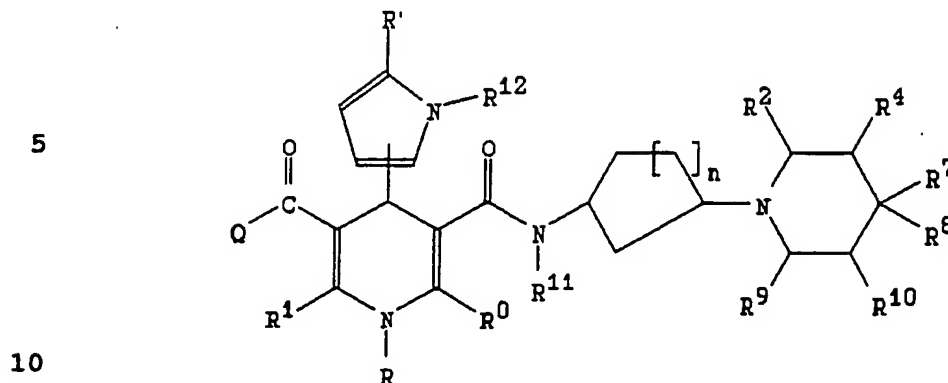
independently the same or different and are H, or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $CONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; wherein j is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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63. A compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰, R¹ and R' are independently the same or different and are

20 H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched

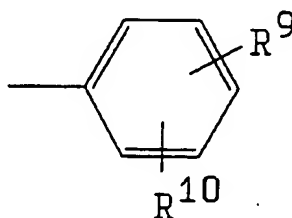
25 chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched

30 chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or

35 a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group;

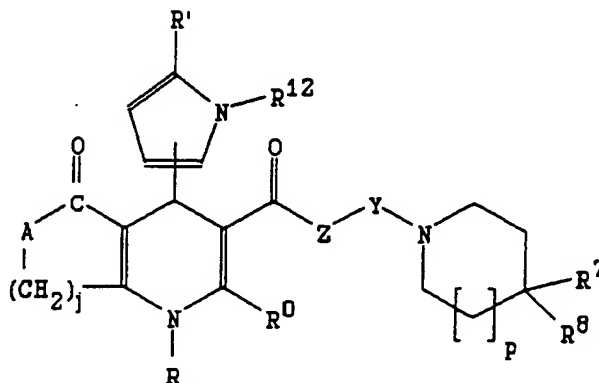
-638-

wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; and wherein n is 0, 1, 2, 3 or 4.

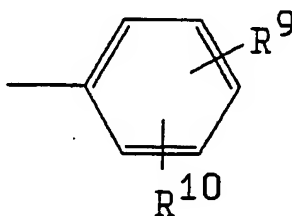
64. A compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or -

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$(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH_2 , CR^a_2 , NH , NR^a , NCHO , NCOR^a , NOH , O or S , where R^a is a methyl, ethyl or propyl group; wherein Z is O , NH , NCHO , NCOR^b , NR^b , NOR^b , or CH_2 , where R^b is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R' are independently the same or different and are H , a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR'_2 , NHOH , $\text{N}^+\text{R}'_3\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O , S or NH , where W^1 is NH_2 , NHR' , NR'_2 , NHOH , $\text{N}^+\text{R}'_3\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are H , CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

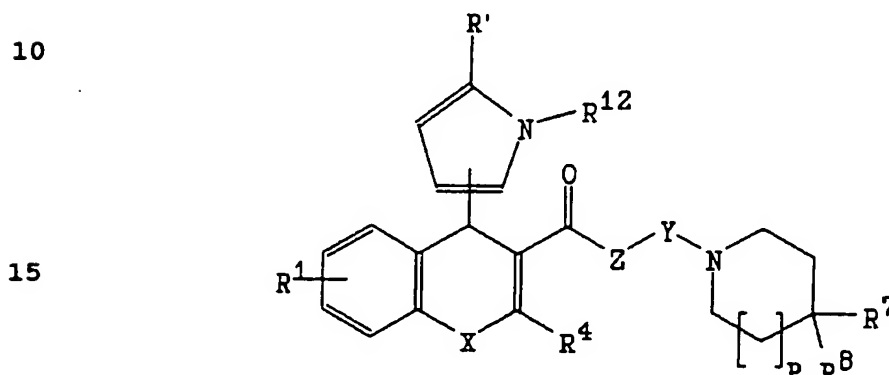


wherein R^9 and R^{10} are independently the same or different and are H , Cl , Br , I , F , OH , NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} ,

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$\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 where R' is a linear or branched chain alkyl group, and
 R^{iv} is a linear or branched chain alkyl group, and q is 2,
 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl or
 5 acyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3
 or 4; and wherein p is 0, 1, 2 or 3.

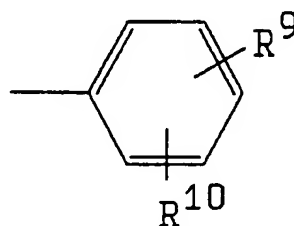
65. A compound having the structure:



wherein X is NH , NR^{a} , O , or S , where R^{a} is H or a linear
 or branched chain alkyl or acyl group, or an aryl group;
 20 wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-$
 $\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or
 different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the
 same or different and are 1, 2, 3 or 4; wherein Z is O,
 25 NH , NCHO , NCOR' , NR' , NOR' , or CH_2 , where R' is a methyl,
 ethyl or propyl group; wherein R^{a} is H, or a linear or

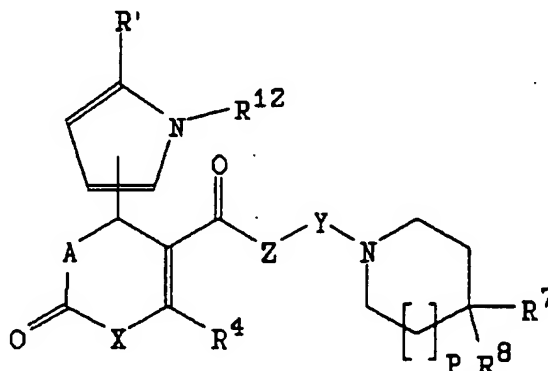
-641-

branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

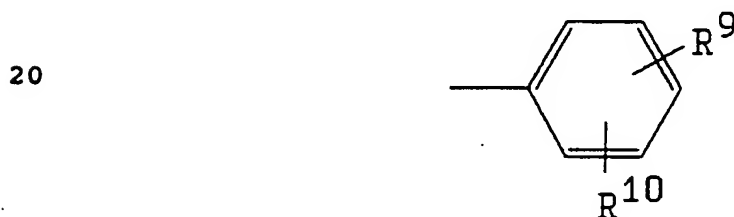
66. A compound having the structure:



wherein A is CH_2 , CR'_2 , NH , NR' , $NCHO$, $NCOR'$, NOH , O or S , where R' is a methyl, ethyl or propyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and

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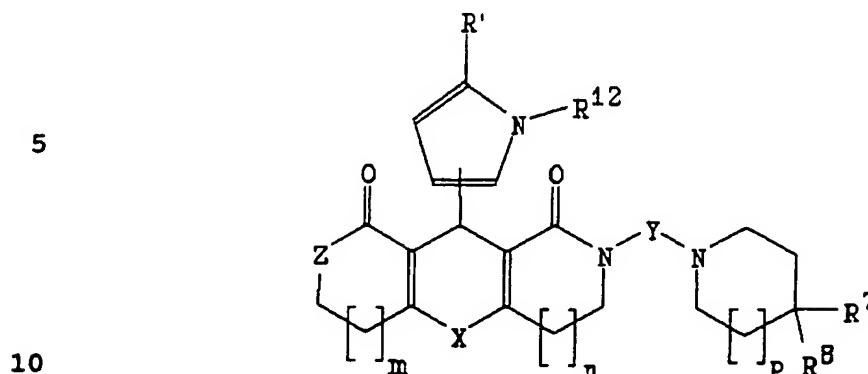
are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR'', NR'', NOR'', or CH₂, where R'' is a methyl, ethyl or propyl group; wherein X is NH, NR^a, O, or S, where R^a is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, or a methyl, ethyl or propyl group; wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² is H or a linear chain alkyl or acyl group; and wherein p is 0, 1, 2 or 3.

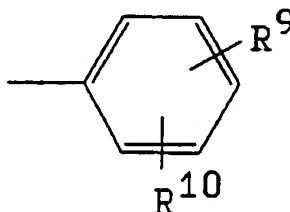
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67. A compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-$, $O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR', or CH_2 , where R' is a methyl, ethyl or propyl group; wherein X is NH, NR'', O, or S, where R'' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R' is H, or a methyl, ethyl or propyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

30

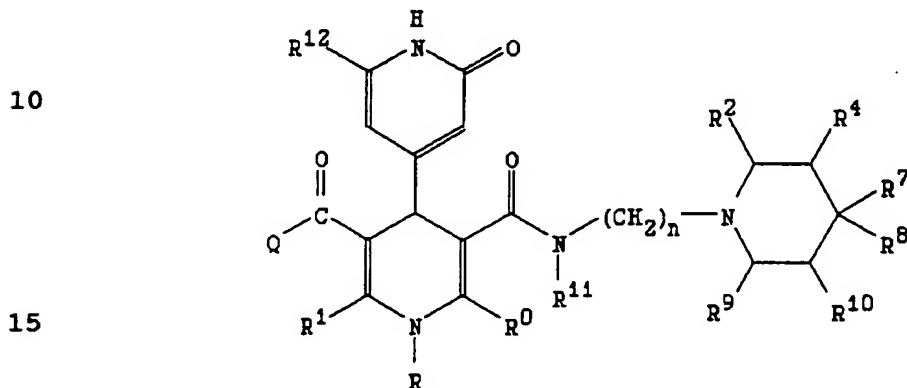


35 wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv},

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where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² is H or a linear chain alkyl or acyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

68. A compound having the structure:

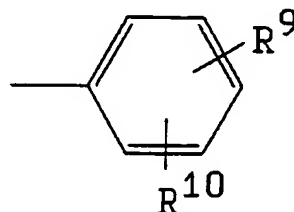


wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR₂'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰, and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3,

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4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, or a linear or branched chain alkyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR', OCOR', NH_2 , NHR', NR'_2 , NHCOR', $CONH_2$, CONHR', $CONR'_2$, COOH, COOR', CHO, COR', COSH, COSR', $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

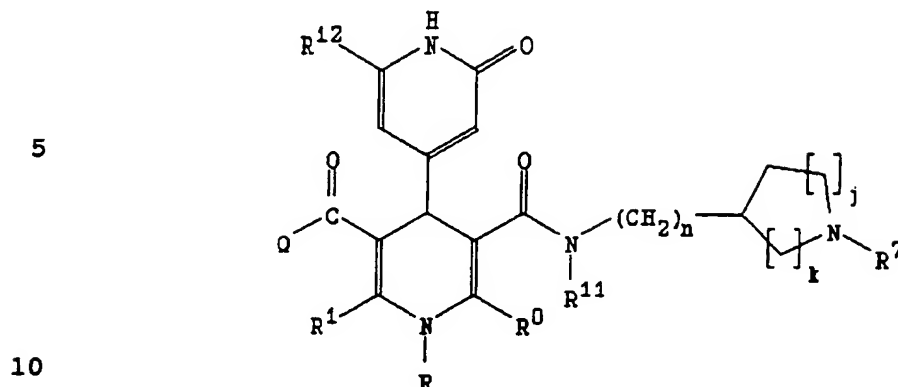
20



25 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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69. A compound having the structure:

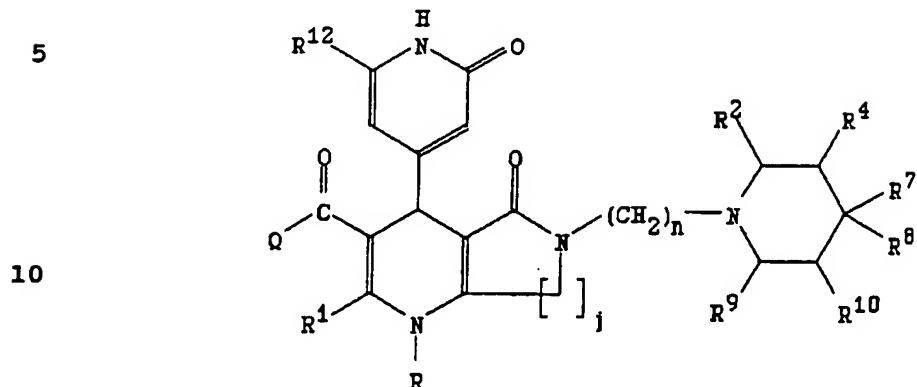


wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR₂', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ is an aryl or diarylalkyl group; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or

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4; and wherein n is 2, 3 or 4.

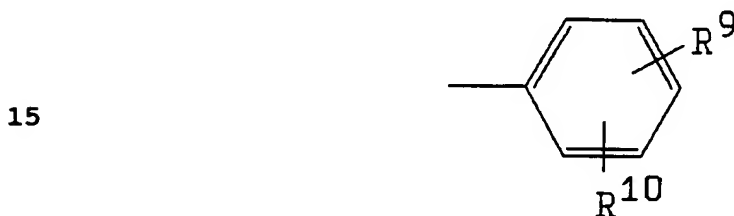
70. A compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'',
 15 NR''OH, NR''OR''', or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl
 group, or an aryl group, where R'' is H, a linear or
 branched chain alkyl group, trialkylsilylalkyl,
 cyanoalkyl, or an aryl group, and R''' is a linear or
 20 branched chain alkyl group, or an aryl group; wherein R
 is H or a linear or branched chain alkyl or acyl group,
 or an aryl group; wherein R¹ is H, a linear or branched
 chain alkyl, an alkoxyalkyl, azidoalkyl,
 aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl,
 25 aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW,
 where W is NH₂, NHR', NR₂', NHOH, N'R₃'Z', NHCOR', N₃, NO₂
 or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl
 group, or an aryl group, where R' is a linear or branched
 30 chain alkyl group, or an aryl group, where W⁰ is O, S or
 NH, where W¹ is NH₂, NHR', NR₂', NHOH, N'R₃'Z', NHCOR', N₃
 or NO₂, and where R' is a linear or branched chain alkyl
 group, or an aryl group, where Z' is a pharmaceutically
 acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v
 35 is 2, 3, 4, 5 or 6; wherein R², R⁹ and R¹⁰ are independ-
 ently the same or different and are H or a linear or
 branched chain alkyl group; wherein R⁴ is H or a linear or

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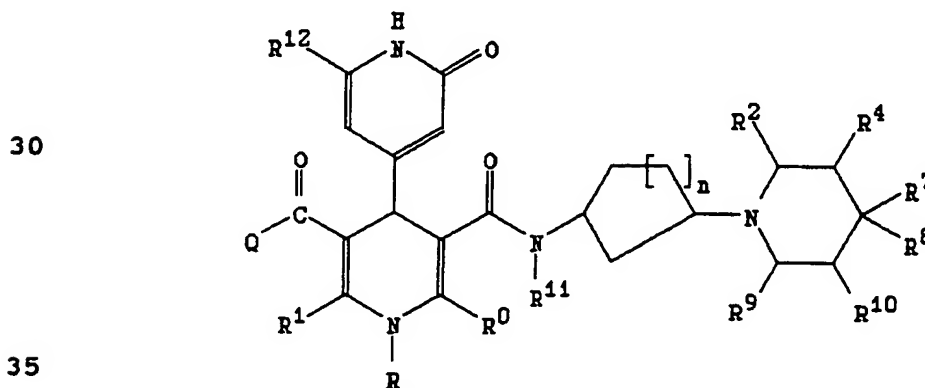
branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H,
 5 CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl,
 10 indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$,
 20 $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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71. A compound having the structure:



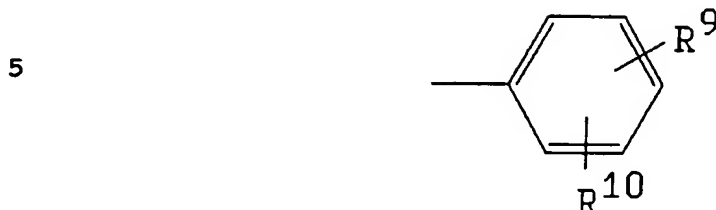
wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR'_2''' ,

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$\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR_2' , NHCOR' , CONH_2 , CONHR' , CONR_2' , COOH , COOR' , CHO, COR' , COSH, COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,

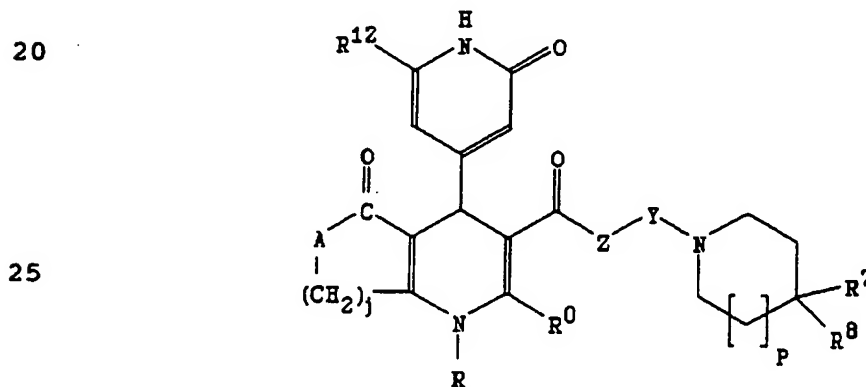
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furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} ,
 $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 where R' is a linear or branched chain alkyl group, and
 R^{iv} is a linear or branched chain alkyl group, and q is 2,
 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group;
 15 wherein R^{12} is H or a linear chain alkyl or acyl group;
 and wherein n is 0, 1, 2, 3 or 4.

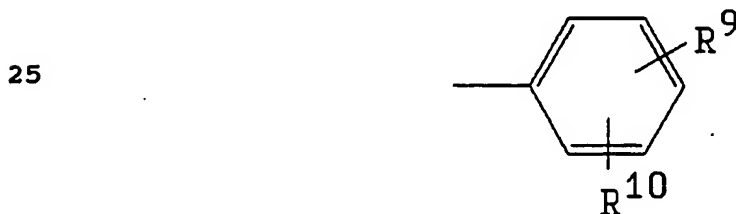
72. A compound having the structure:



wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-$
 30 $\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or
 different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the
 same or different and are 1, 2, 3 or 4; wherein A is CH_2 ,
 CR'_2 , NH, NR' , NCHO , NCOR' , NOH , O or S, where R' is a
 35 methyl, ethyl or propyl group; wherein Z is O, NH, NCHO ,
 NCOR'' , NR'' , NOR'' , or CH_2 , where R'' is a methyl, ethyl
 or propyl group; wherein R is H or a linear or branched

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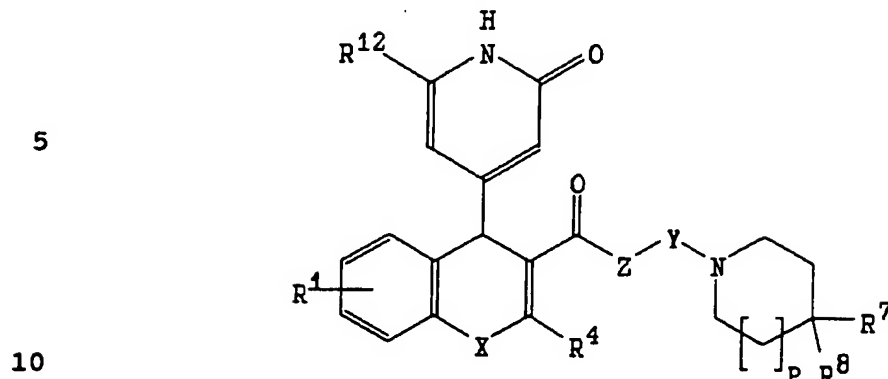
chain alkyl or acyl group, or an aryl group; wherein R^0 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:



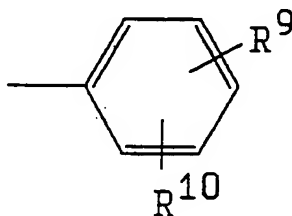
wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

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73. A compound having the structure:



wherein X is NH, NR'', O or S, where R'' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or
15 different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR', NOR' or CH₂, where R' is a methyl, ethyl or propyl group; wherein R¹ is H, Cl, Br, I, F, NO₂,
20 CN, OH, OR², OCOR², NH₂, NR², NHCOR₂, or CF₃, where R² is a linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR',
25 OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,
30 quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



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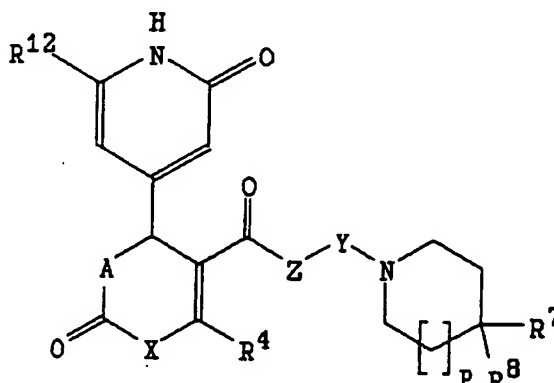
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

74. A compound having the structure:

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wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein X is NH , NR'' , O or S , where R'' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR_2' , NHCOR' , CONH_2 , CONHR' , CONR_2' , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

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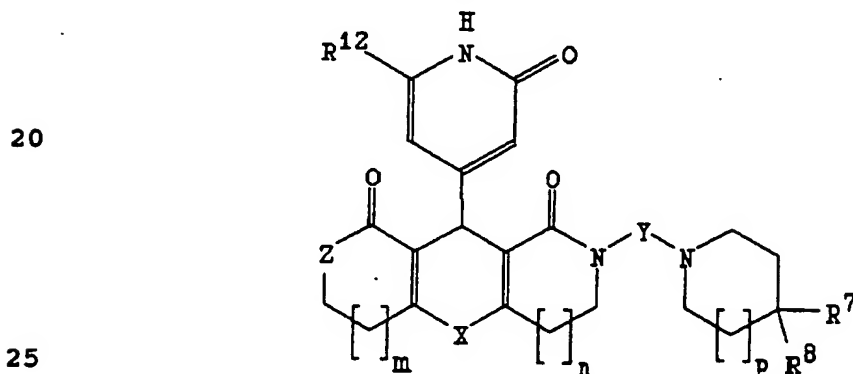
group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

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75. A compound having the structure:



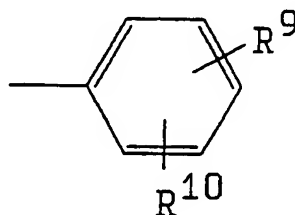
wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein X is NH, NR' , O, or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a

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benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

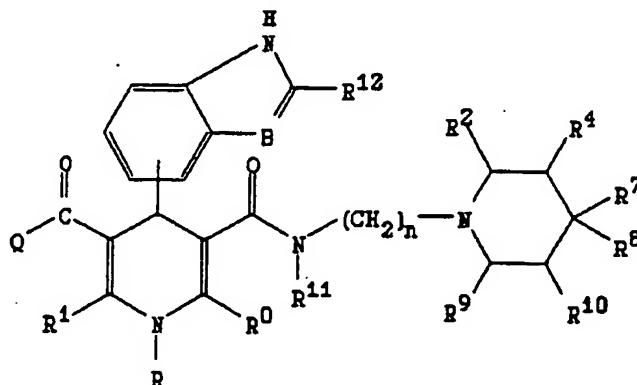


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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

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76. A compound having the structure:



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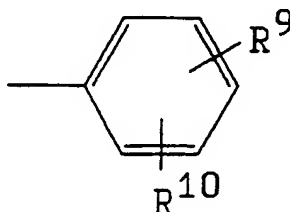
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wherein B is CH or N; wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and

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R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-
 5 alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxy-alkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group,
 10 where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and
 15 t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched
 20 chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$,
 25 $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_q OH$ or $COO(CH_2)_q OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene
 30 group, or an aryl group having the structure:



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wherein R^9 and R^{10} are independently the same or different

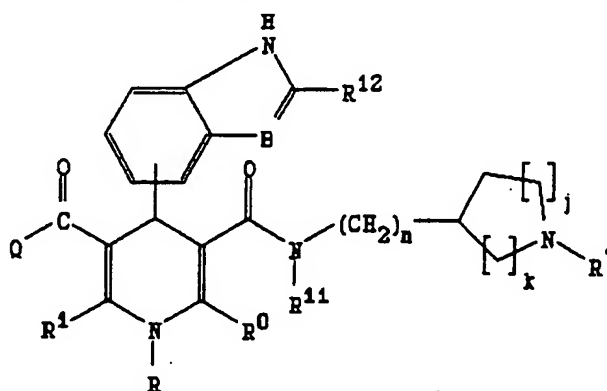
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and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

77. A compound having the structure:

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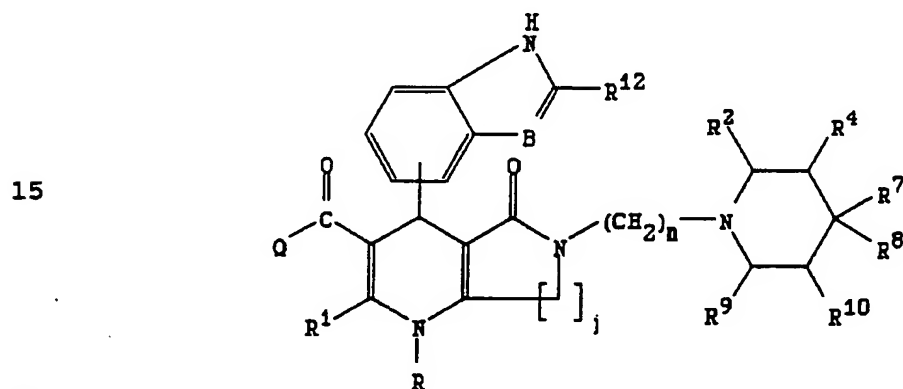


20 wherein B is CH or N; wherein Q is OH, OR'', SH, SR''', NH₂, NHR'', NR₂'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and
 25 R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-
 30 alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxy-alkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group,
 35 where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a

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linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 is an aryl or diarylalkyl group; wherein R^{11} is a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

78. A compound having the structure:

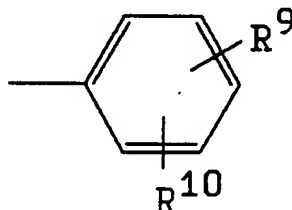


wherein B is CH or N; wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a

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linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

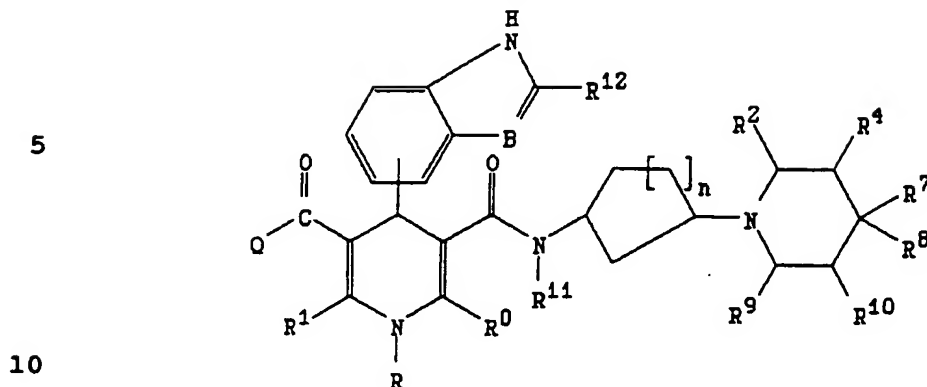
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25 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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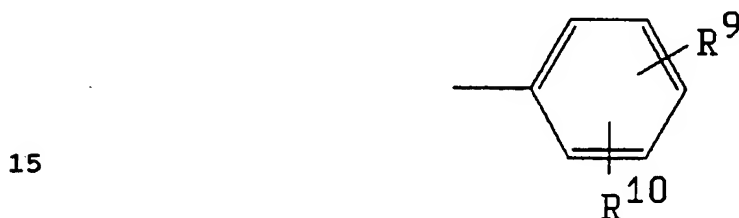
79. A compound having the structure:



wherein B is CH or N; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a

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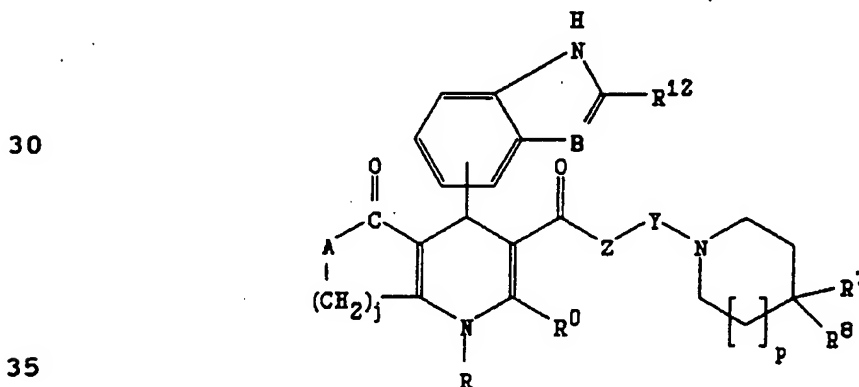
hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$,
 5 $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 10 group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$,
 20 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; and n is 2, 3 or 4.

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80. A compound having the structure:



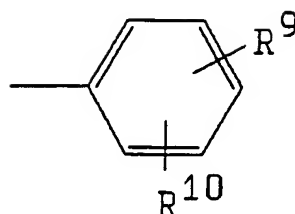
wherein A is CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S,

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where R is a methyl, ethyl or propyl group; wherein B is CH or N; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^0 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the

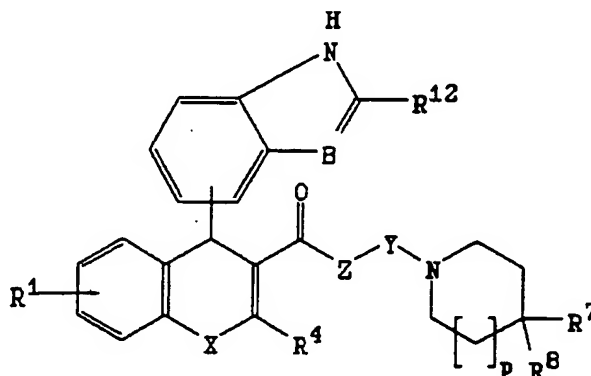
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structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

81. A compound having the structure:

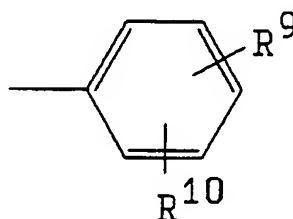


wherein B is CH or N; wherein X is NH, NR' , O, or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^1 is H, Cl, Br, I, F, NO_2 , CN, OH, OR^2 , OCOR^2 , NH_2 , NR^2 , NHCOR_2 or CF_3 , where R^2 is a linear or branched chain alkyl group, or an aryl group; wherein R^4 is H, or a linear or

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branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$,
 5 $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

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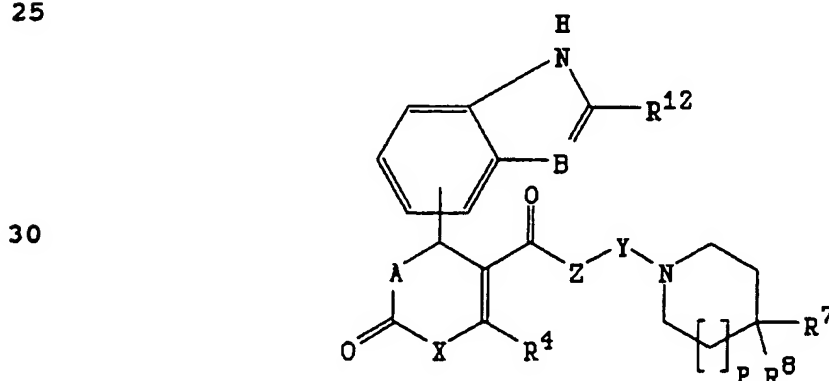


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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and
 20 R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

82. A compound having the structure:

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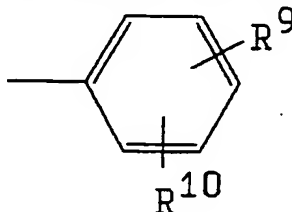


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wherein A is CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; B is CH or N; where Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-$ O- $(CH_2)_k-$, where h and k are independently the same or
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different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl
 5 or propyl group; wherein X is NH, NR' , O or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 ,
 10 OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,
 15 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

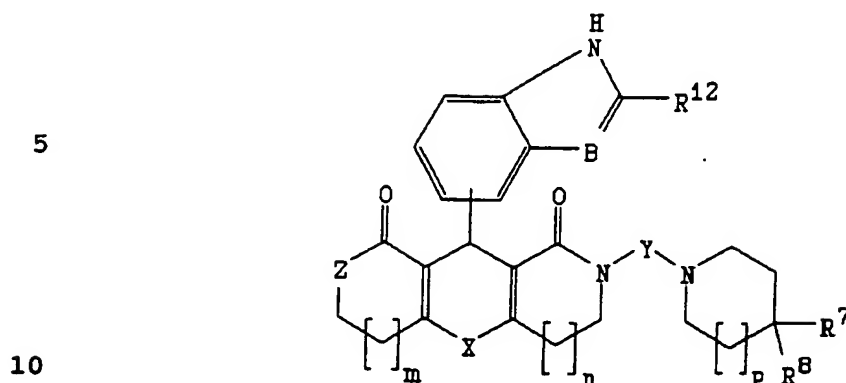


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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $CONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$,
 25 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

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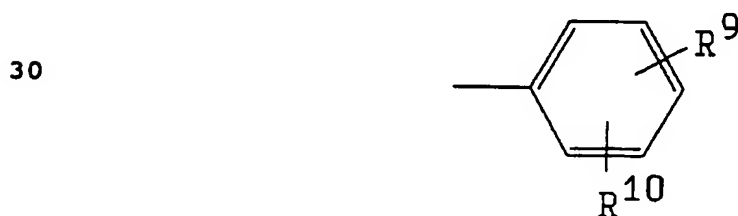
83. A compound having the structure:



wherein B is CH or N; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein X is NH, NR' , O or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, COOH, $COOR'$, CHO, COR' , COSH, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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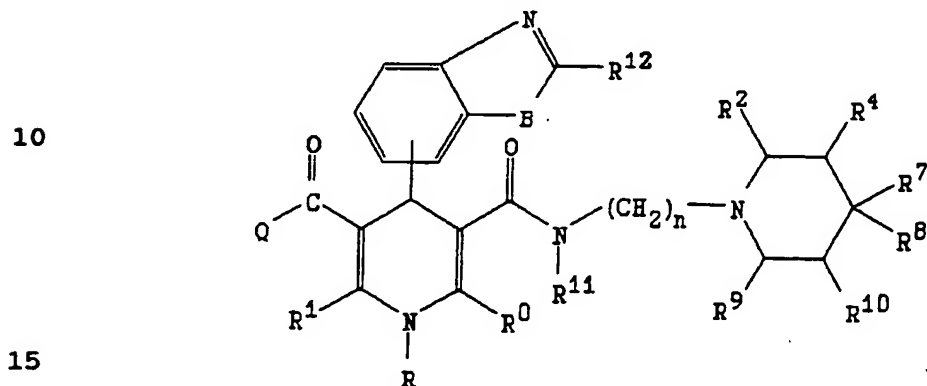
wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and

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R^{1v} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

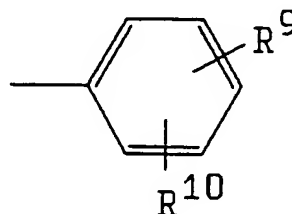
84. A compound having the structure:



wherein B is O or S; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein

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R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

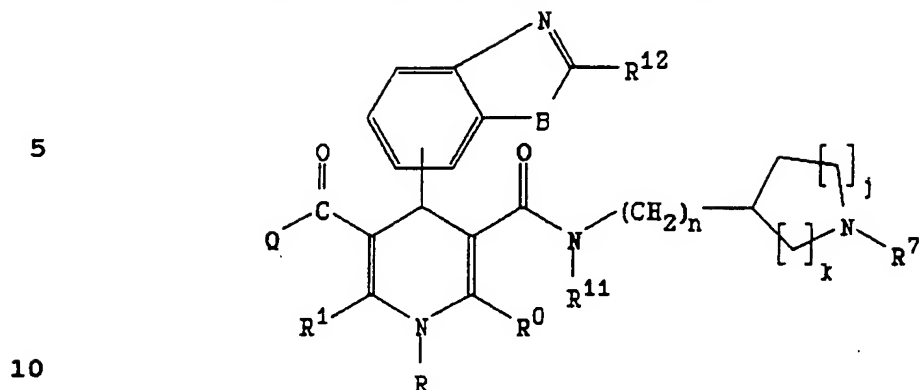


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; and n is 2, 3 or 4.

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85. A compound having the structure:

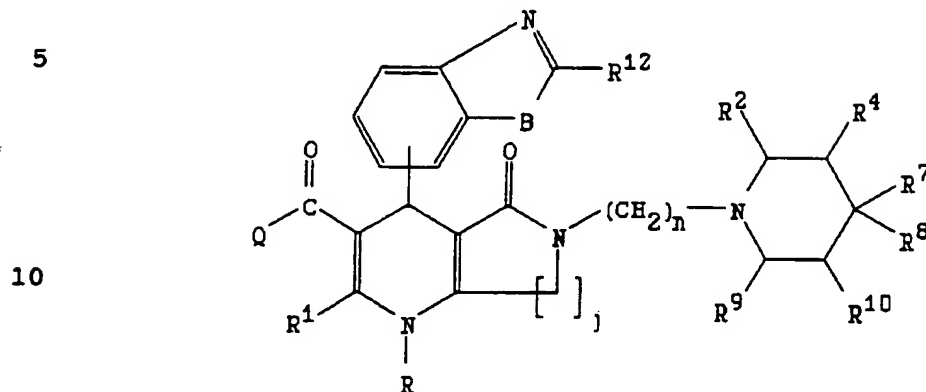


wherein B is O or S; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁷ is an aryl or diarylalkyl group; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0,

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1, 2, 3 or 4; and n is 2, 3 or 4.

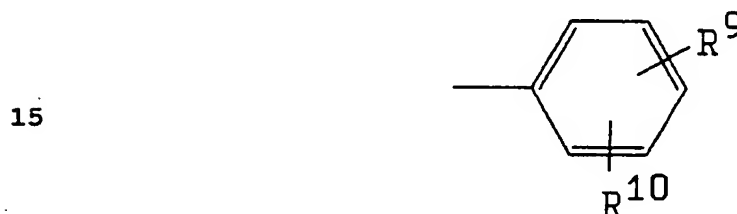
86. A compound having the structure:



wherein B is O or S; wherein Q is OH, OR'', SH, SR''',
 15 NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or
 branched chain alkyl group, or an arylalkyl group, or an
 alkenyl or alkynyl group, or an aryl group, where R'' is
 H, a linear or branched chain alkyl group, trialkyl-
 silylalkyl, cyanoalkyl, or an aryl group, and R''' is a
 20 linear or branched chain alkyl group, or an aryl group;
 wherein R¹ is H, a linear or branched chain alkyl, an
 alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-
 alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxy-
 alkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR',
 25 NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a
 linear or branched chain alkyl group, or an arylalkyl
 group, or an alkenyl or alkynyl group, or an aryl group,
 where R' is a linear or branched chain alkyl group, or an
 aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR',
 30 NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a
 linear or branched chain alkyl group, or an aryl group,
 where Z⁻ is a pharmaceutically acceptable counterion, and
 t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein
 R is H or a linear or branched chain alkyl or acyl group,
 35 or an aryl group; wherein R², R⁹ and R¹⁰ are independently
 the same or different and are H or a linear or branched
 chain alkyl group; wherein R⁴ is H or a linear or branched

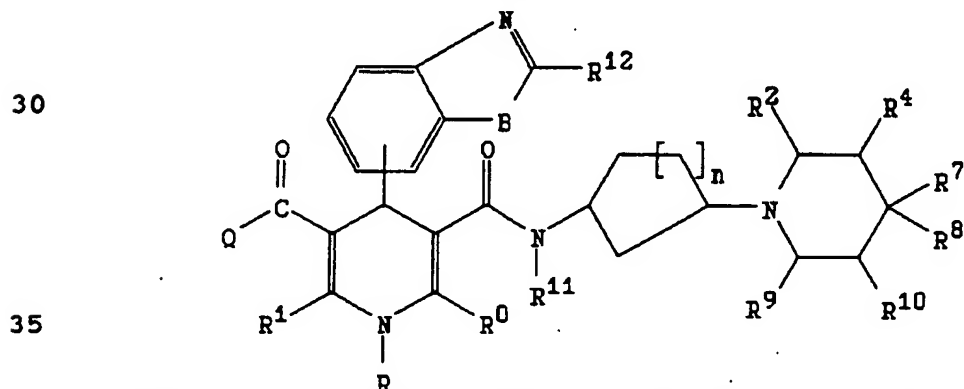
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chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 ,
 5 OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl,
 10 quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$,
 20 $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; wherein j
 25 is 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

87. A compound having the structure:



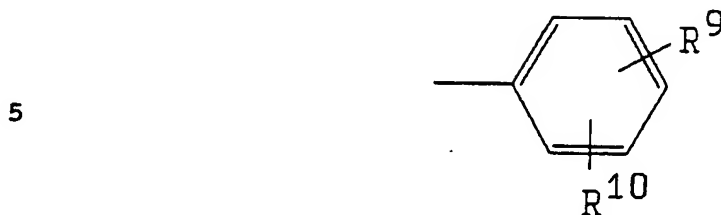
wherein B is O or S; wherein Q is OH, OR'' , SH, SR''' ,

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NH_2 , NHR'''' , NR_2'''' , $\text{NR}'''\text{OH}$, $\text{NR}'''\text{OR}''''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR_2' , NHCOR' , CONH_2 , CONHR' , CONR_2' , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

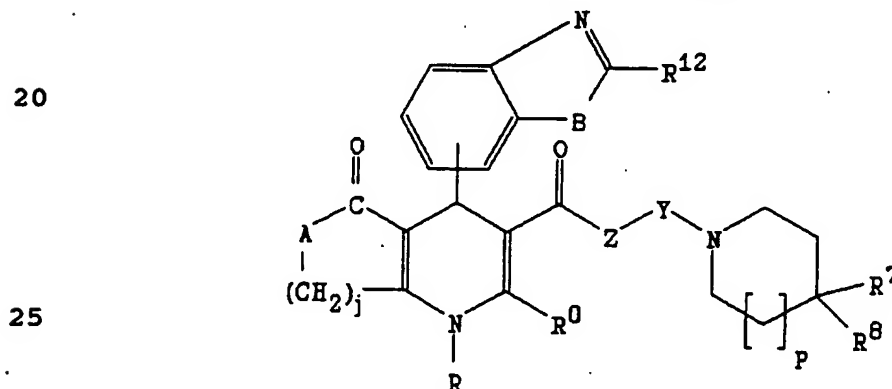
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group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl or acyl group; and wherein n is 0, 1, 2, 3 or 4.

88. A compound having the structure:

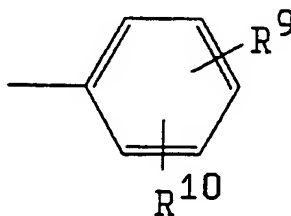


wherein B is O or S; wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' ,

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NHOH, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH_2 , CR_2' , NH , NR' , $NCHO$, $NCOR'$, NOH , O or S , where R' is a methyl, ethyl or propyl group; wherein Z is O , NH , $NCHO$, $NCOR^a$, NR^a , NOR^a , or CH_2 , where R^a is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H , CN , CF_3 , OH , OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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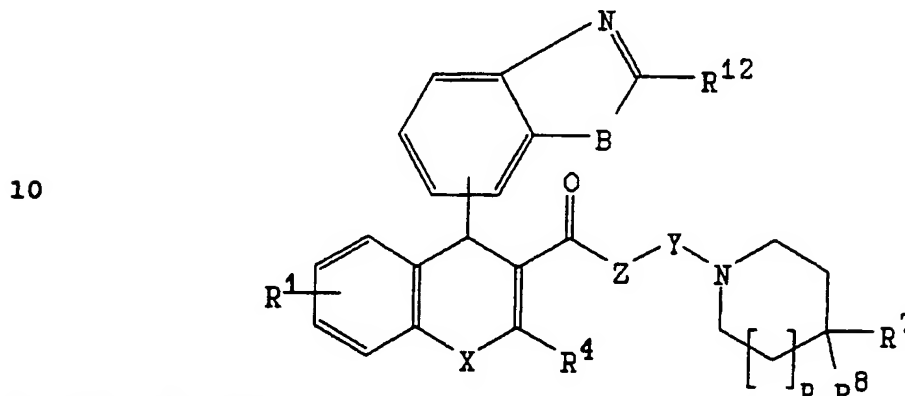
wherein R^9 and R^{10} are independently the same or different and are H , Cl , Br , I , F , OH , NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR_2^{iv} , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and

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R^{IV} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

5 89. A compound having the structure:



15 wherein B is O or S; wherein X is NH, NR' , O, or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^1 is H, Cl, Br, I, F, NO_2 , CN, OH, OR^2 , $OCOR^2$, NH_2 , NR^2 , $NHCOR^2$, CF_3 , where R^2 is a linear or branched chain alkyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, COOH, $COOR'$, CHO, COR' , COSH, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or

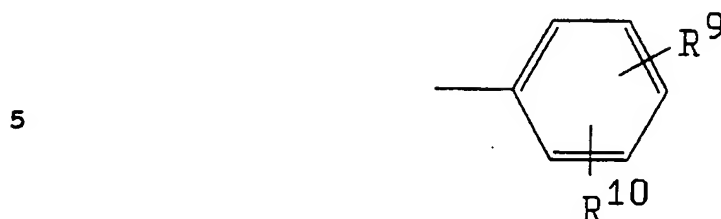
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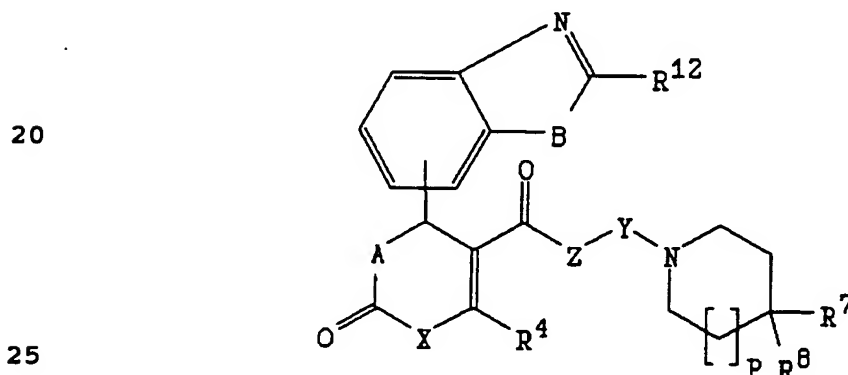
thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv_2} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

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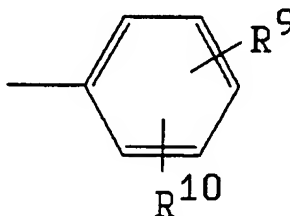
90. A compound having the structure:



wherein A is CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein B is O or S; wherein X is NH, NR' , O, or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^4 is H, or a

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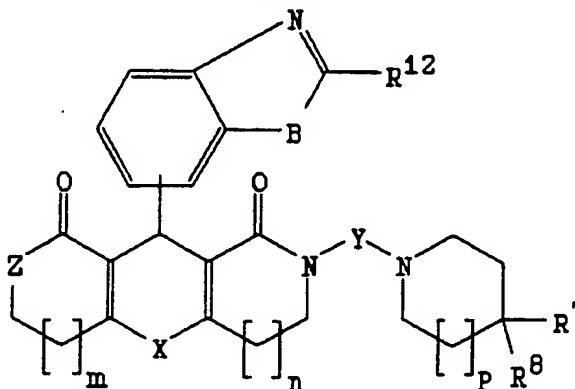
linear or branched chain alkyl group, or an aryl group;
 wherein R^7 and R^8 are independently the same or different
 and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 ,
 $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' ,
 5 $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl
 group, a linear or branched chain alkyl or cycloalkyl
 group, or are a heteroaryl group comprising a pyridyl,
 indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,
 furyl or thiophene group, or an aryl group having the
 10 structure:



15

wherein R^9 and R^{10} are independently the same or different
 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$,
 $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$,
 20 where R' is a linear or branched chain alkyl group, and
 R^{iv} is a linear or branched chain alkyl group, and q is 2,
 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group;
 and wherein p is 0, 1, 2 or 3.

25 91. A compound having the structure:



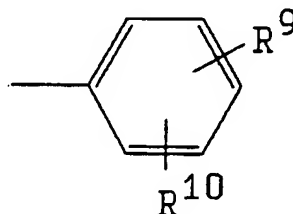
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35

wherein B is O or S; wherein X is NH, NR' , O or S, where
 R' is H or a linear or branched chain alkyl or acyl

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group, or an aryl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



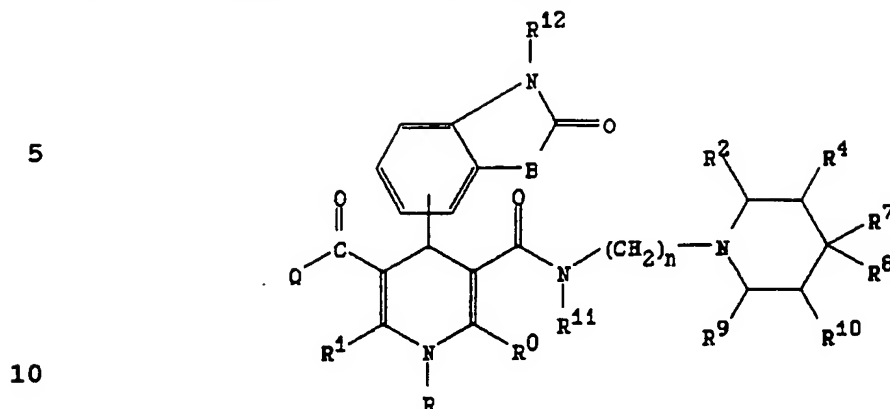
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

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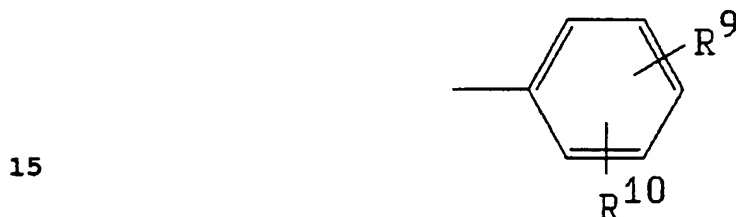
92. A compound having the structure:



wherein B is O, S or NR^{12} ; wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a

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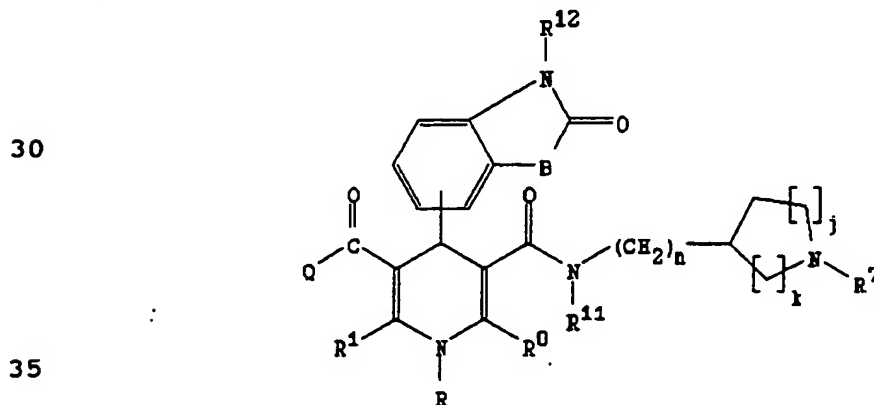
hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$,
 5 $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene
 10 group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$,
 20 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; and n is 2, 3 or 4.

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93. A compound having the structure:

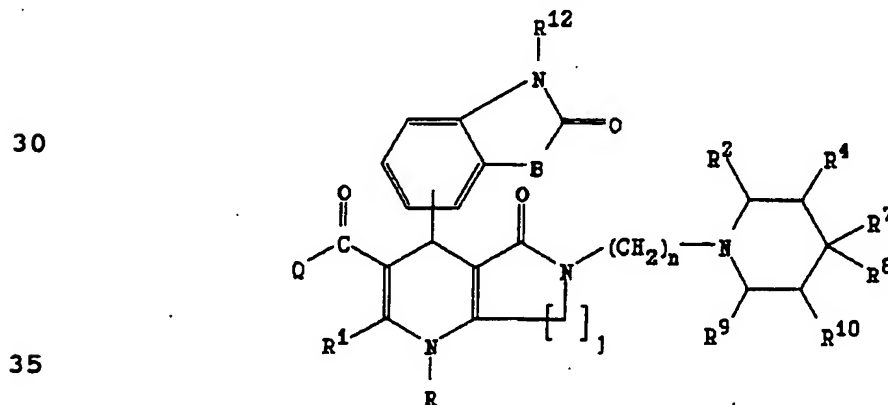


wherein B is O, S or N^{12} ; wherein Q is OH, OR'' , SH,

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SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R⁷ is an aryl or diarylalkyl group; wherein R¹¹ is a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and n is 2, 3 or 4.

94. A compound having the structure:



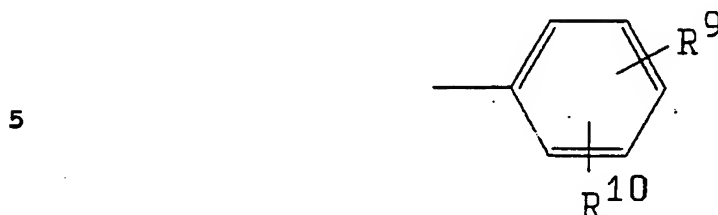
wherein B is O, S or N¹²; wherein Q is OH, OR'', SH,

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SR'''' , NH_2 , NHR'''' , NR_2'''' , $NR''OH$, $NR''OR''''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkyl-
 5 silylalkyl, cyanoalkyl, or an aryl group, and R'''' is a linear or branched chain alkyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxy-
 10 alkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an
 15 aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein
 20 R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a
 25 hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$
 30 or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

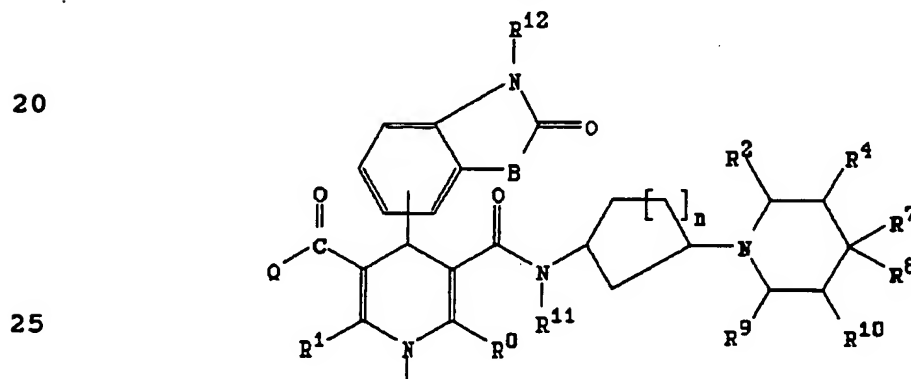
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group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv}_2 , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; and n is 2, 3 or 4.

95. A compound having the structure:



wherein B is CH or N^{R} ; wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxy-

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alkyl, or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group,

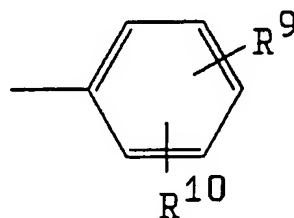
5 where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and

10 t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is a linear or branched

15 chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR_2' , NHCOR' , CONH_2 , CONHR' ,

20 CONR_2' , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene

25 group, or an aryl group having the structure:



30 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,

35 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group;

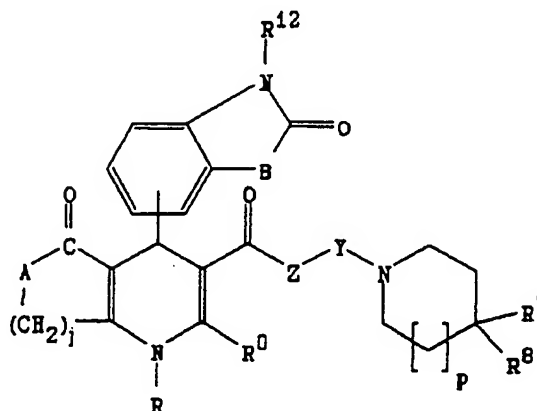
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wherein R^{12} is H or a linear chain alkyl or acyl group;
wherein j is 1, 2, 3 or 4; and n is 0, 1, 2, 3 or 4.

96. A compound having the structure:

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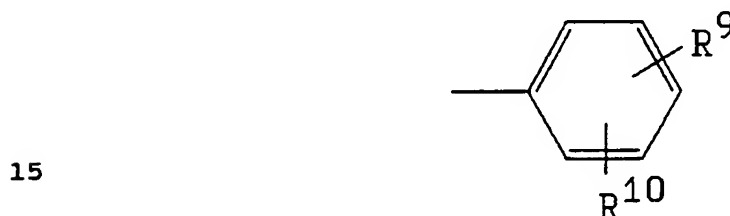
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15 wherein B is O, S, or NR' , where R' is H or a linear chain alkyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and
20 k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH_2 , CR'_2 , NH, NR' , $NCHO$, $NCOR'$, NOH , O or S, where R' is a methyl, ethyl or propyl group; wherein Z is O, NH, $NCHO$, $NCOR''$, NR'' , NOR'' , or CH_2 , where R'' is a methyl, ethyl or propyl group; wherein R
25 is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 is independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azido-alkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxy-alkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an
30 aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group,

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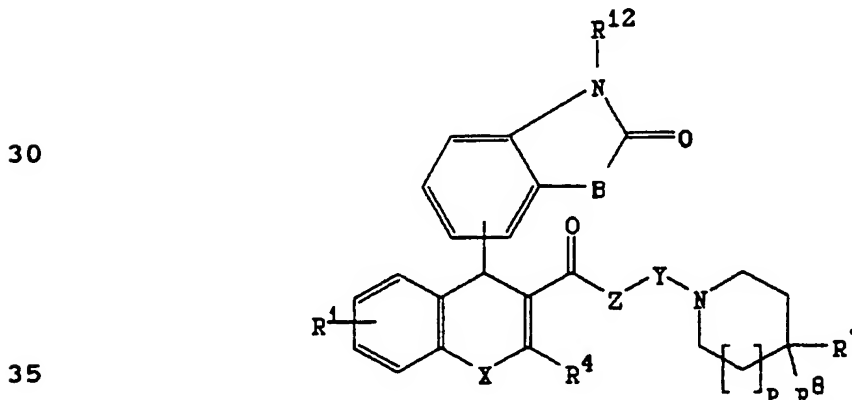
where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$,
 5 $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or
 10 thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $CONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$,
 20 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

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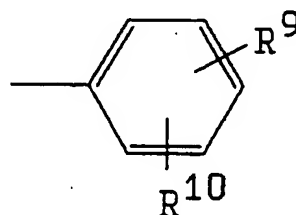
97. A compound having the structure:



wherein B is O, S or NR' , where R' is H or a linear chain

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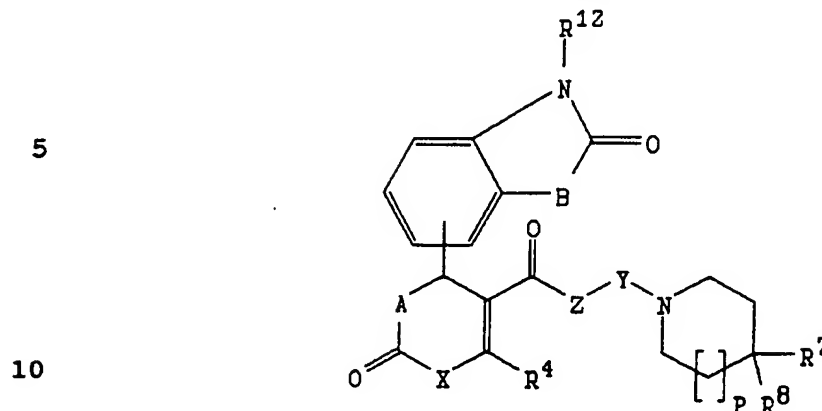
alkyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein R^1 is H, Cl, Br, I, F, NO_2 , CN, OH, OR^2 , $OCOR^2$, NH_2 , NR^2 , $NHCOR^2$ or CF_3 , where R^2 is a linear or branched chain alkyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, COOH, $COOR'$, CHO, COR' , COSH, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

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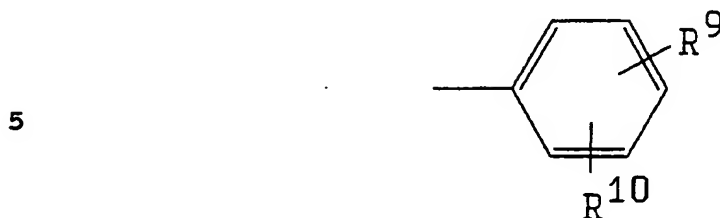
98. A compound having the structure:



wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; B is O , S or NR' , where R' is H or a linear chain alkyl group; wherein
15 Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO ,
20 NCOR'' , NR'' , NOR'' or CH_2 , where R'' is a methyl, ethyl or propyl group; wherein X is NH , NR' , O or S , where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^4 is H , or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are
25 independently the same or different and are H , CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl
30 group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene

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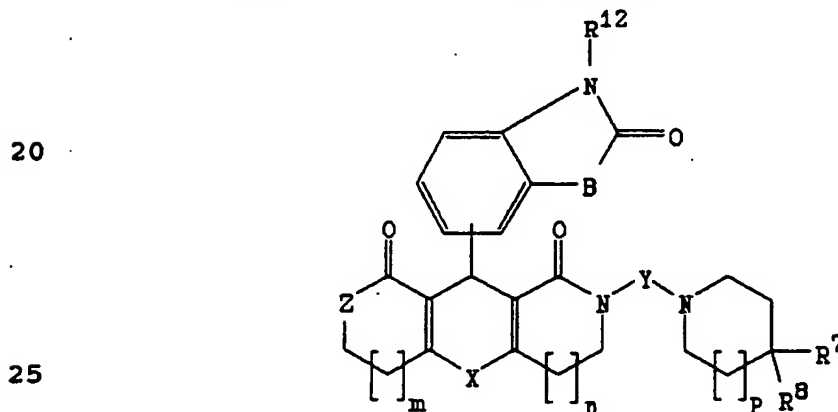
group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, 10 $CONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

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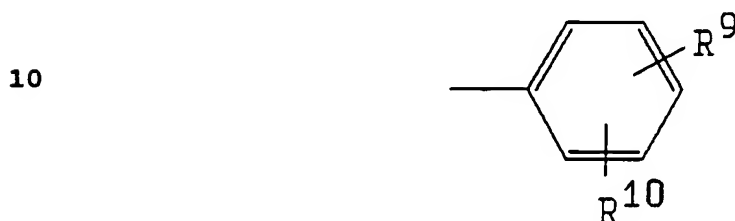
99. A compound having the structure:



wherein B is O, S or NR', where R' is H or a linear chain alkyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein X is NH, NR', O or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R' and R⁸ are independently the same or different and are H, CN, CF₃,

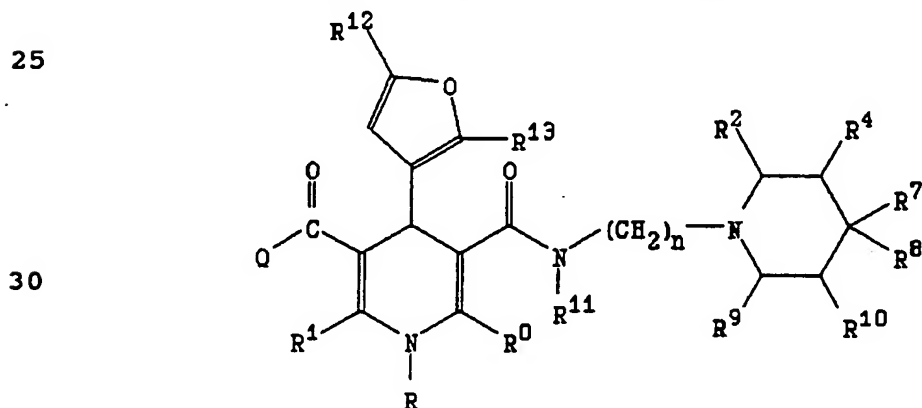
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OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR',
 CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH
 or COO(CH₂)_qOR', or a benzyl group, a linear or branched
 chain alkyl or cycloalkyl group, or are a heteroaryl
 5 group comprising a pyridyl, indolyl, indolylalkyl,
 quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 15 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv},
 OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv},
 where R' is a linear or branched chain alkyl group, and
 R^{iv} is a linear or branched chain alkyl group, and q is 2,
 3, 4 or 5; wherein R¹² is H or a linear chain alkyl group;
 20 wherein m and n are independently the same or different
 and are 0 or 1; and wherein p is 0, 1, 2 or 3.

100. A compound having the structure:



wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR''₂,
 35 NR''OH, NR''OR'', or a linear or branched chain alkyl
 group, or an arylalkyl group, or an alkenyl or alkynyl
 group, or an aryl group, where R'' is H, a linear or

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branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H,

5 a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched

10 chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched

15 chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or

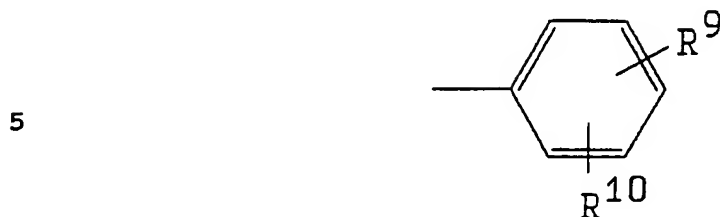
20 different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are independ-

25 ently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl

30 group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

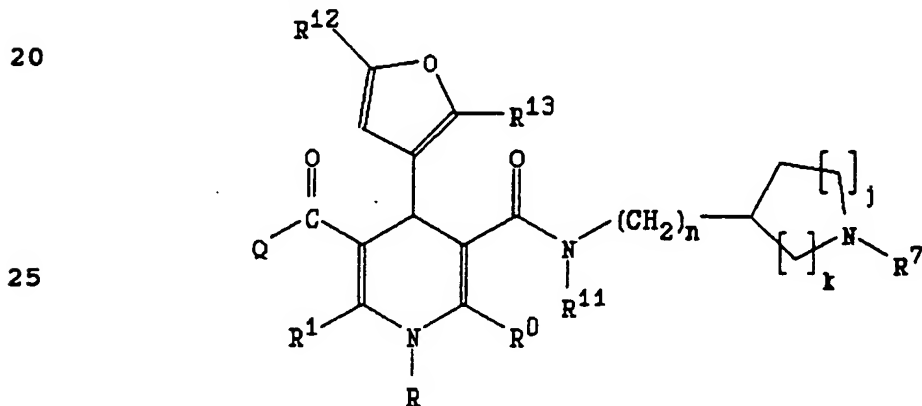
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group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$,
 10 where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different
 15 and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

101. A compound having the structure:



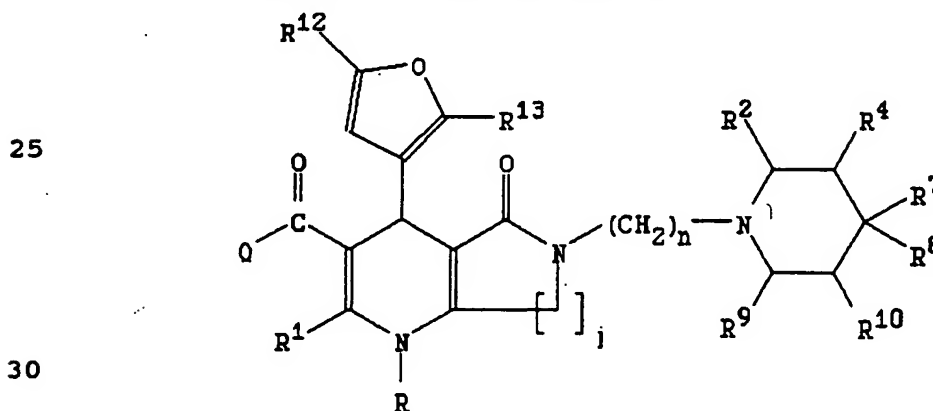
wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' ,
 30 $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or
 35 branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azido-

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alkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_t\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_v\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 is an aryl or diarylalkyl group; wherein R^{11} is a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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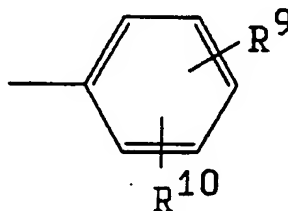
102. A compound having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or

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branched chain alkyl group, or an aryl group; wherein R^1 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2 W^0 (CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3 Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_q OH$ or $COO(CH_2)_q OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$,

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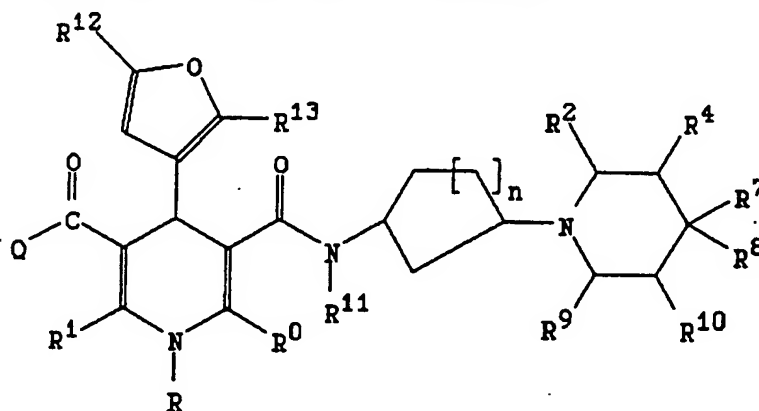
$\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{ii} is H or a linear chain alkyl group;

5 wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

103. A compound having the structure:

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20 wherein Q is OH , OR'' , SH , SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}'''\text{OH}$, $\text{NR}'''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl,

25 cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl,

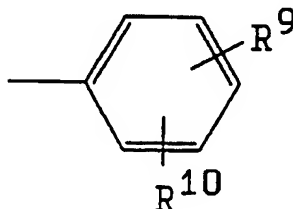
30 trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(\text{CH}_2)_n\text{W}$, where W is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 , NO_2 or $\text{CH}_2\text{W}^0(\text{CH}_2)_m\text{W}^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear

35 or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , NHOH , $\text{N}^+\text{R}_3'\text{Z}^-$, NHCOR' , N_3 or NO_2 , and where R' is a linear or branched

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chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or different and are a linear or branched chain alkyl group; wherein R⁴ is a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

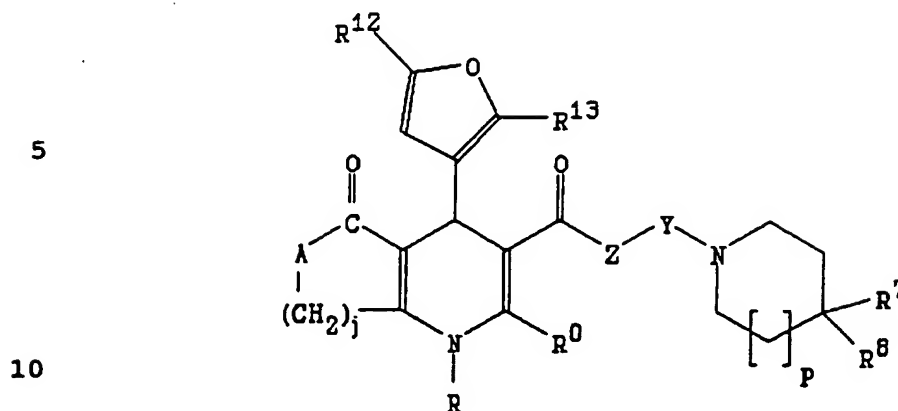
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25 wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, ORⁿ, OCORⁿ, OCOORⁿ, OCONHRⁿ, NH₂, NHRⁿ, NRⁿ₂, NHCORⁿ, NHCOORⁿ or NHCONHRⁿ, where R' is a linear or branched chain alkyl group, and Rⁿ is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² and R¹³ are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 0, 1, 2, 3 or 4.

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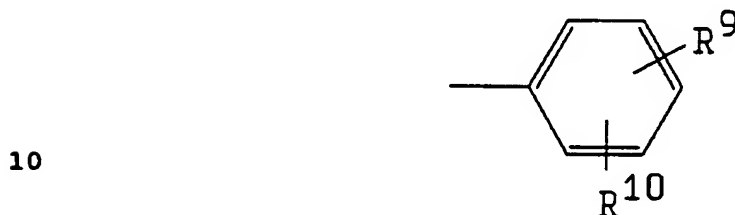
104. A compound having the structure:



wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH_2 , CR'_2 , NH , NR' , $NCHO$, $NCOR'$, NOH , O or S , where R' is a methyl, ethyl or propyl group; wherein Z is O , NH , $NCHO$, $NCOR''$, NR'' , NOR'' or CH_2 , where R'' is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^0 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O , S or NH , where W^1 is NH_2 , NHR' , NR'_2 , $NHOH$, $N^+R'_3Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or

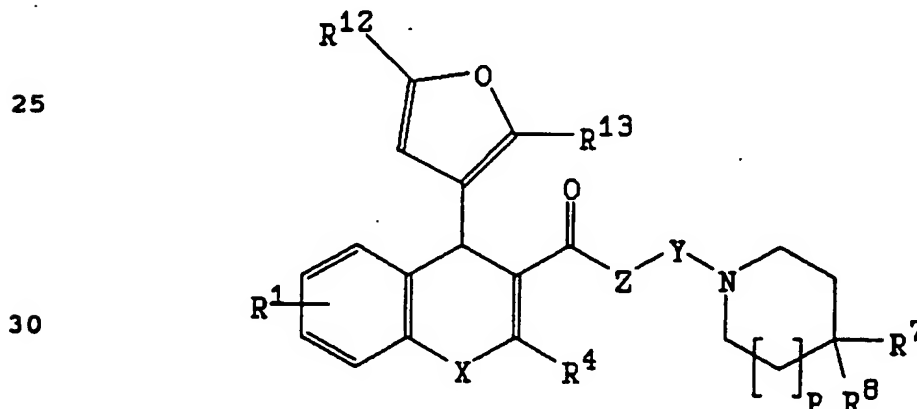
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COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinoliny, isoquinoliny, pyrrol, furyl or thiophene group, or an aryl group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv}, OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where
 15 R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² and R¹³ are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and
 20 wherein p is 0, 1, 2 or 3.

105. A compound having the structure:



wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or
 35 different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O,

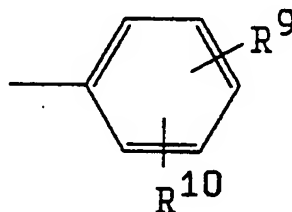
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NH, NCHO, NCOR, NR, NOR or CH₂, where R is a methyl, ethyl or propyl group; wherein R¹ is H, Cl, Br, I, F, NO₂, CN, OH, OR², OCOR², NH₂, NR², NHCOR₂, or CF₃, where R² is a linear or branched chain alkyl group, or an aryl group;

5 wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or

10 COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

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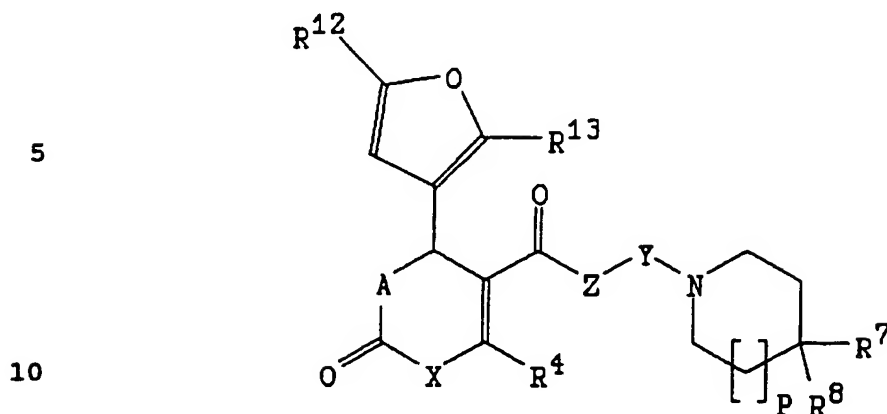
wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^w, OCOR^w, OCOOR^w, OCONHR^w, NH₂, NHR^w, NR^w₂, NHCOR^w, NHCOOR^w or NHCONHR^w, where

25 R' is a linear or branched chain alkyl group, and R^w is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² and R¹³ are independently the same or different and are H or a linear chain alkyl group; and wherein p is 0, 1, 2 or 3.

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106. A compound having the structure:



wherein A is CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S, where R is a methyl, ethyl or propyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR', NR', NOR' or CH_2 , where R' is a methyl, ethyl or propyl group; wherein X is NH, NR'', O or S, where R'' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR', OCOR', NH_2 , NHR', NR', NHCOR', $CONH_2$, CONHR', $CONR'_2$, COOH, COOR', CHO, COR', COSH, COSR', $COO(CH_2)_4OH$ or $COO(CH_2)_4OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

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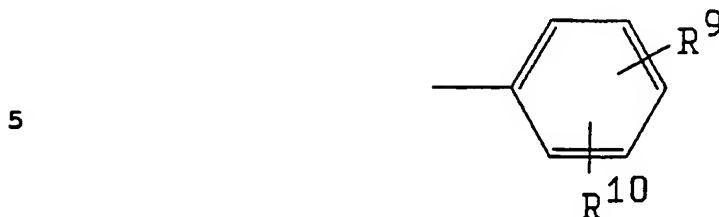
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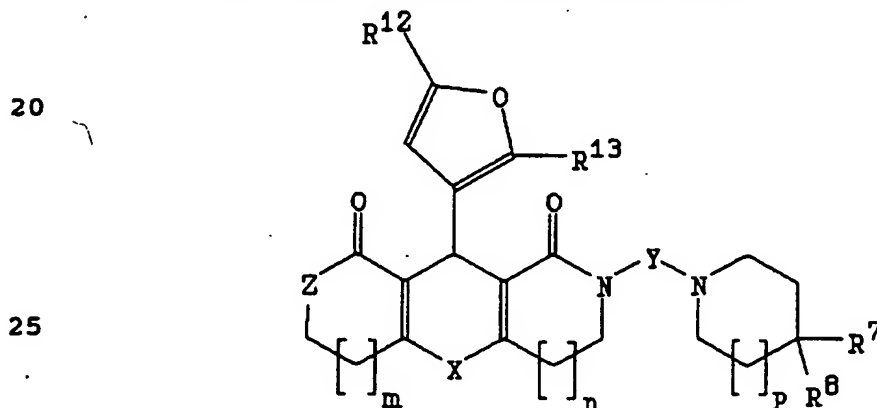
group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR^{iv_2} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and

15 wherein p is 0, 1, 2 or 3.

107. A compound having the structure:



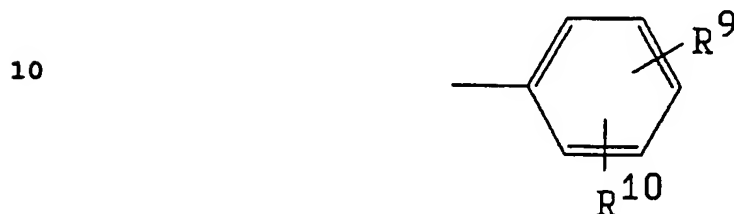
wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-$ $\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR, NR, NOR or CH_2 , where R is a methyl, ethyl or propyl group; wherein X is NH, NR' , O or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 ,

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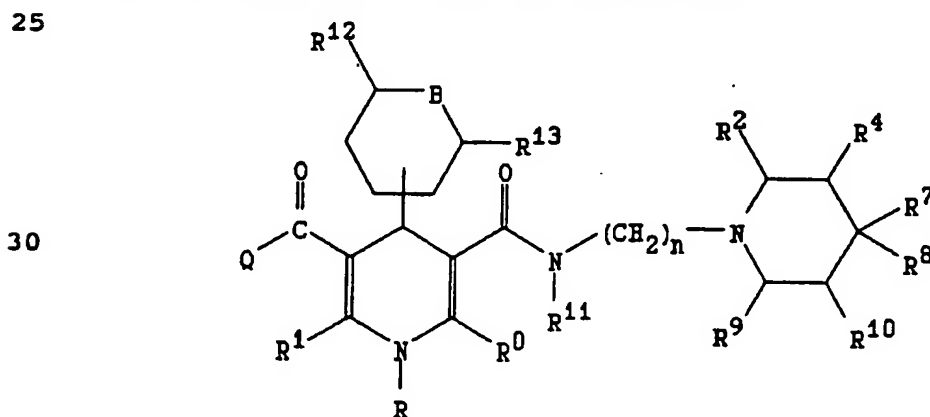
-702-

NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR',
 CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a
 benzyl group, a linear or branched chain alkyl or
 cycloalkyl group, or are a heteroaryl group comprising a
 5 pyridyl, indolyl, indolylalkyl, quinolinyl, isoquin-
 olinyl, pyrrol, furyl or thiophene group, or an aryl
 group having the structure:



wherein R⁹ and R¹⁰ are independently the same or different
 15 and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^{iv}, OCOR^{iv}, OCOOR^{iv},
 OCONHR^{iv}, NH₂, NHR^{iv}, NR^{iv}₂, NHCOR^{iv}, NHCOOR^{iv} or NHCONHR^{iv}, where
 R' is a linear or branched chain alkyl group, and R^{iv} is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R¹² and R¹³ are independently the same or
 20 different and are H or a linear chain alkyl group;
 wherein m and n are independently the same or different
 and are 0 or 1; and wherein p is 0, 1, 2 or 3.

108. A compound having the structure:



35 wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a
 linear or branched chain alkyl group, or OH, ORⁱ, NH₂,
 NRⁱ₂, O(C=O)Rⁱ or NH(C=O)Rⁱⁱ, where Rⁱⁱ is H or a linear

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alkyl group, and where R^b is a linear or branched chain alkyl group; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl

5 or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H,

10 a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z', NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched

15 chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z', NHCOR', N₃ or NO₂, and where R' is a linear or branched

20 chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or

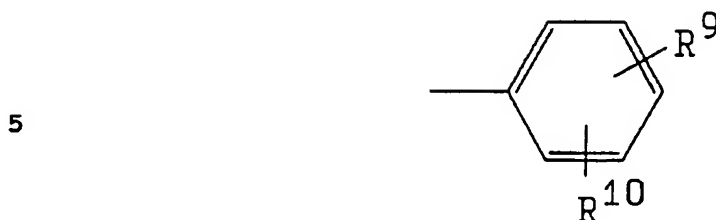
25 different and are H or a linear or branched chain alkyl group; wherein R⁴ is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R⁷ and R⁸ are

30 independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR₂', NHCOR', CONH₂, CONHR', CONR₂', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl

35 group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

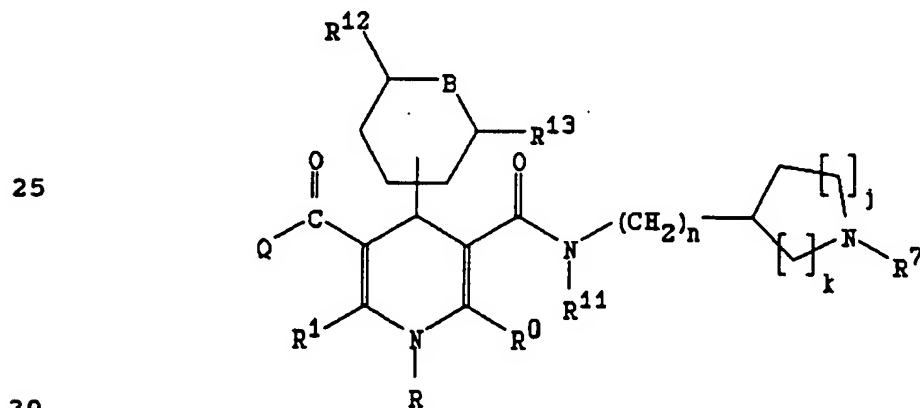
-704-

group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR_2^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where R^v is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

20 109. A compound having the structure:



wherein B is O, S, CH_2 , CHR^a , NH or NR^b , where R^a is a linear or branched chain alkyl group, or OH, OR^c , NH_2 , NR_2^c , $\text{O}(\text{C}=\text{O})\text{R}^c$ or $\text{NH}(\text{C}=\text{O})\text{R}^c$, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein Q is OH, $\text{OR}^{''}$, SH, $\text{SR}^{'''}$, NH_2 , $\text{NHR}^{'''}$, $\text{NR}_2^{'''}$, $\text{NR}^{''}\text{OH}$, $\text{NR}^{''}\text{OR}^{'''}$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or

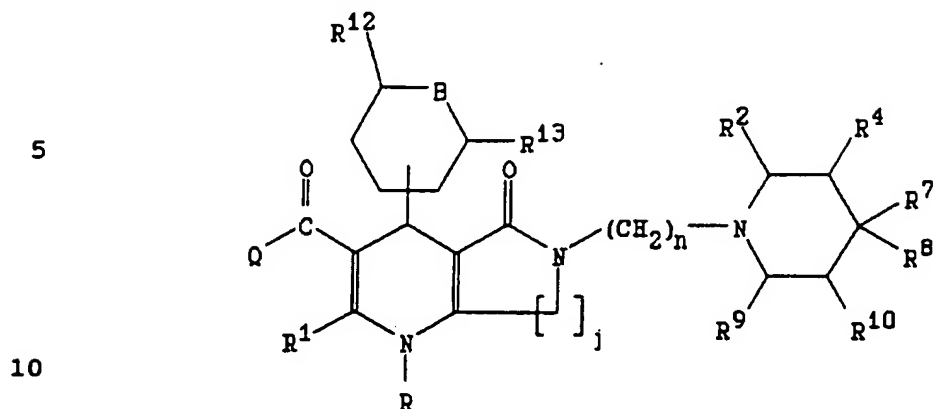
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alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^7 is an aryl or diarylalkyl group; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; and wherein n is 2, 3 or 4.

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110. A compound having the structure:

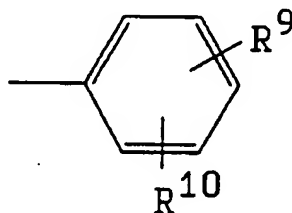


wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched chain alkyl group, or OH, OR^c, NH₂, NR₂^c, O(C=O)R^c or NH(C=O)R^c, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein Q is OH, OR^{''}, SH, SR^{'''}, NH₂, NHR^{'''}, NR₂^{'''}, NR^{''}OH, NR^{''}OR^{'''}, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R^{''} is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R^{'''} is a linear or branched chain alkyl group, or an aryl group; wherein Rⁱ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR['], NR₂['], NHOH, N⁺R₃[']Z⁻, NHCOR['], N₃, NO₂ or CH₂W⁰(CH₂)_vWⁱ, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R['] is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where Wⁱ is NH₂, NHR['], NR₂['], NHOH, N⁺R₃[']Z⁻, NHCOR['], N₃ or NO₂, and where R['] is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R⁹ and R¹⁰ are independently the same or

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different, and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

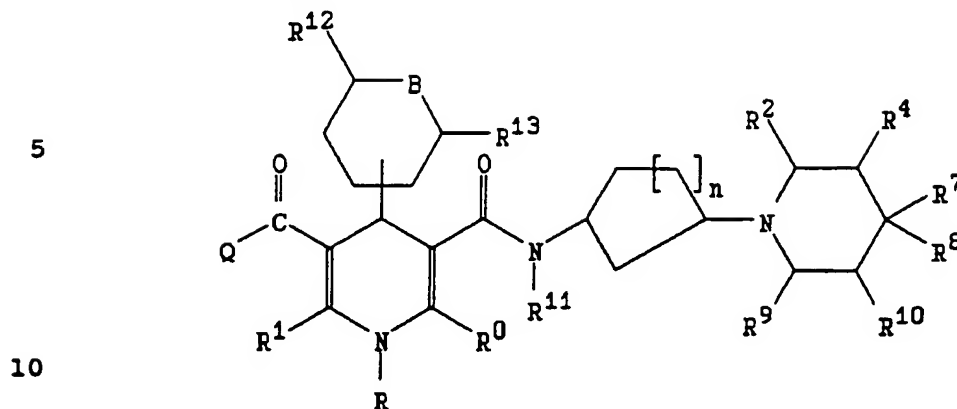
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20 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4
 25 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

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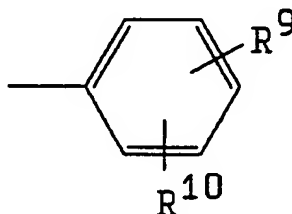
111. A compound having the structure:



wherein B is O , S , CH_2 , CHR^a , NH or NR^b , where R^a is a linear or branched chain alkyl group, or OH , OR^c , NH_2 , NR_2^c , $O(C=O)R^c$ or $NH(C=O)R^c$, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein Q is OH , OR'' , SH , SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H , a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H , a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_t W$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 , or $CH_2W^0(CH_2)_v W^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O , S or NH , where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl

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group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

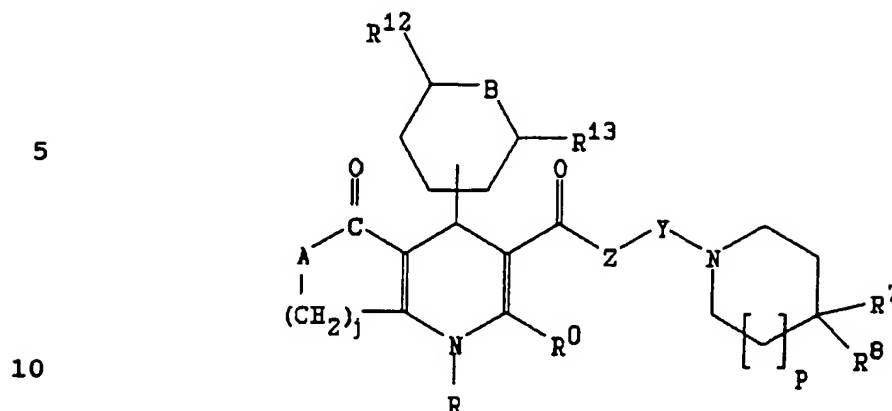


wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; and wherein n is 0, 1, 2, 3 or 4.

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112. A compound having the structure:

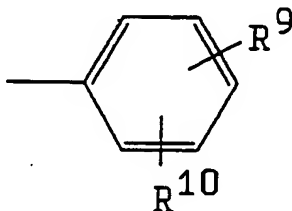


wherein B is O, S, CH_2 , CHR^a , NH or NR^b , where R^a is a linear or branched chain alkyl group, or OH, OR^c , NH_2 , NR_2^c , $O(C=O)R^c$ or $NH(C=O)R^c$, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein Y is $-(CH_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(CH_2)_h-O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH_2 , CR_2' , NH, NR' , NCHO, $NCOR'$, NOH, O or S, where R' is a methyl, ethyl or propyl group; wherein Z is O, NH, NCHO, $NCOR''$, NR'' , NOR'' or CH_2 , where R'' is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl, or acyl group, or an aryl group; wherein R^0 is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_tW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z is a pharmaceutically acceptable counterion, and t is 1, 2, 3,

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- 4, 5 or 6 and v is 2, 3, 4, 5 or 6; H, or a linear or branched chain, alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, alkyl group, or an aryl group;
- 5 wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl
- 10 group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

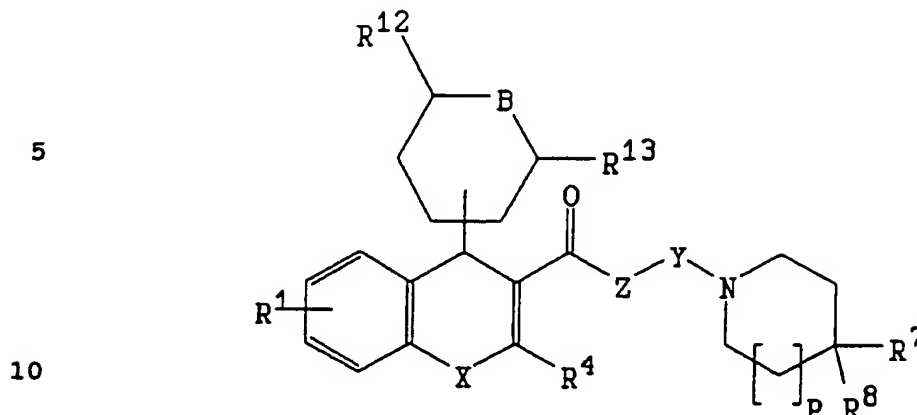
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- 20 wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v, OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4
- 25 or 5; wherein R¹² and R¹³ are independently the same or different and are H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein n is 2, 3 or 4; and wherein p is 0, 1, 2 or 3.

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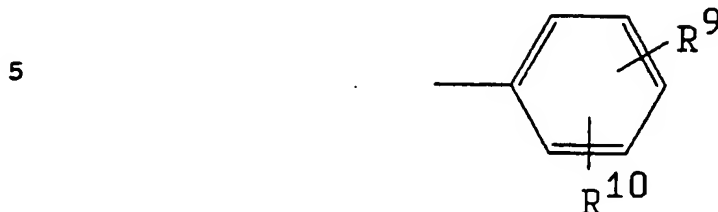
113. A compound having the structure:



wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched chain alkyl group, or OH, OR^c, NH₂, NR^c, O(C=O)R^c or NH(C=O)R^c, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein X is NH, NR', O or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR'', NR'', NOR'' or CH₂, where R'' is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹ is H, Cl, Br, I, F, NO₂, CN, OH, OR², OCOR², NH₂, NR², NHCOR₂ or CF₃, where R² is a linear or branched chain alkyl group, or an aryl group; wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,

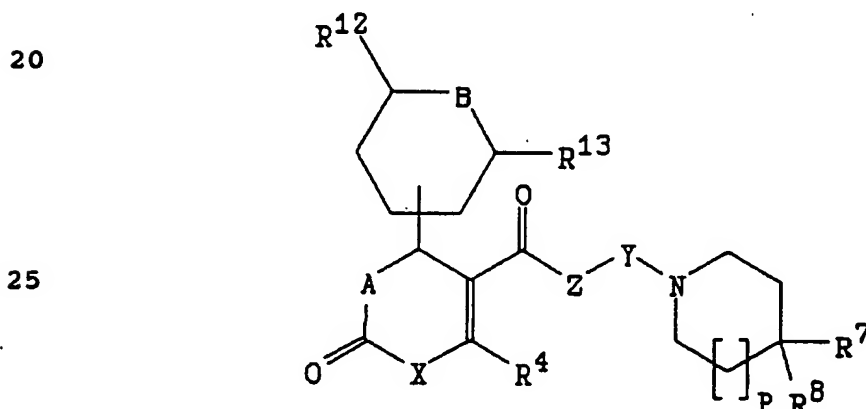
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furyl or thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different
 10 and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v ,
 OCONHR^v , NH_2 , NHR^v , NR_2^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where
 R^v is a linear or branched chain alkyl group, and R^v is
 a linear or branched chain alkyl group, and q is 2, 3, 4
 or 5; wherein R^{12} and R^{13} are independently the same or
 15 different and are H or a linear chain alkyl group; and
 wherein p is 0, 1, 2 or 3.

114. A compound having the structure:

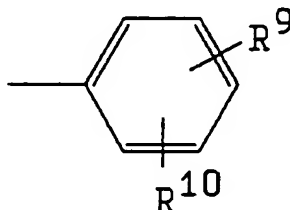


wherein A is CH_2 , CR_2 , NH, NR, NCHO, NCOR, NOH, O or S,
 30 where R is a methyl, ethyl or propyl group; B is O, S,
 CH_2 , CHR^a , NH or NR^b , where R^a is a linear or branched
 chain alkyl group, or OH, OR^c , NH_2 , NR_2^c , $\text{O}(\text{C}=\text{O})\text{R}^c$ or
 $\text{NH}(\text{C}=\text{O})\text{R}^c$, where R^c is H or a linear alkyl group, and
 where R^b is a linear or branched chain alkyl group;
 35 wherein X is NH, NR' , O or S, where R' is H or a linear
 or branched chain alkyl or acyl group, or an aryl group;
 wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_n-$

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$O-(CH_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(CH_2)_h-CH=CH-(CH_2)_k-$; or $-(CH_2)_h-C\equiv C-(CH_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O,
 5 NH, NCHO, NCOR'', NR'', NOR'' or CH₂, where R'' is a methyl, ethyl or propyl group; wherein R⁴ is H, or a linear or branched chain alkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂,
 10 NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol,
 15 furyl or thiophene group, or an aryl group having the structure:

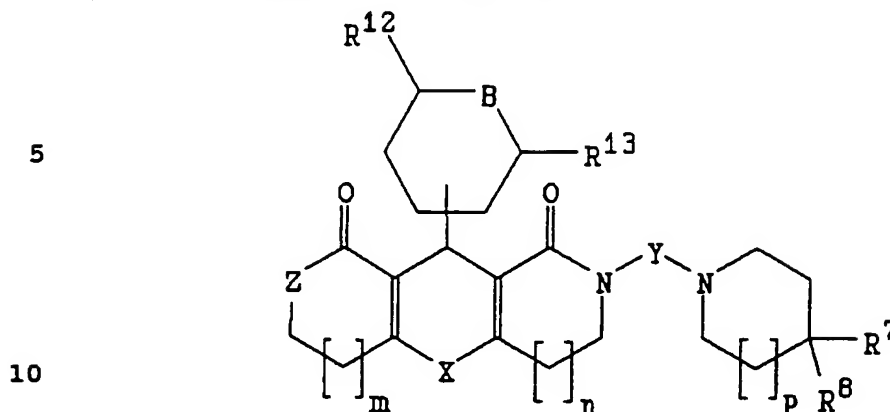
20



wherein R⁹ and R¹⁰ are independently the same or different and are H, Cl, Br, I, F, OH, NO₂, N₃, OR^v, OCOR^v, OCOOR^v,
 25 OCONHR^v, NH₂, NHR^v, NR^v₂, NHCOR^v, NHCOOR^v or NHCONHR^v, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R¹² and R¹³ are independently the same or different and are H or a linear chain alkyl group; and
 30 wherein p is 0, 1, 2 or 3.

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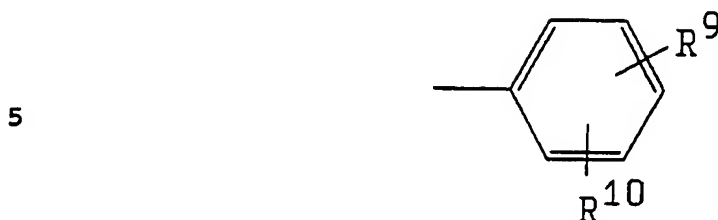
115. A compound having the structure:



wherein B is O, S, CH₂, CHR^a, NH or NR^b, where R^a is a linear or branched chain alkyl group, or OH, OR^c, NH₂, NR^c, O(C=O)R^c or NH(C=O)R^c, where R^c is H or a linear alkyl group, and where R^b is a linear or branched chain alkyl group; wherein X is NH, NR', O or S, where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR'', NR'', NOR'' or CH₂, where R'' is a methyl, ethyl or propyl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR', NHCOR', CONH₂, CONHR', CONR', COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)_qOH or COO(CH₂)_qOR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

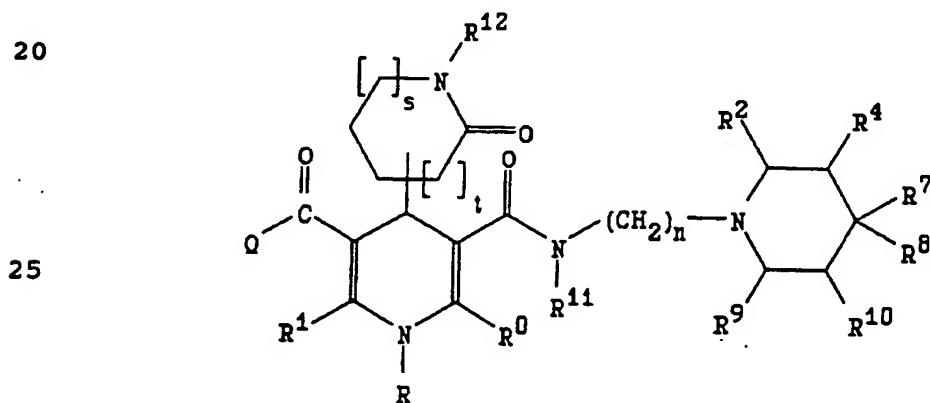
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group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , OCOR^{iv} , OCOOR^{iv} , $\text{OCONHR}^{\text{iv}}$, NH_2 , NHR^{iv} , NR_2^{iv} , NHCOR^{iv} , $\text{NHCOOR}^{\text{iv}}$ or $\text{NHCONHR}^{\text{iv}}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} and R^{13} are independently the same or different and are H or a linear chain alkyl group; wherein m and n are independently the same or different and are 0 or 1; and wherein p is 0, 1, 2 or 3.

116. A compound having the structure:

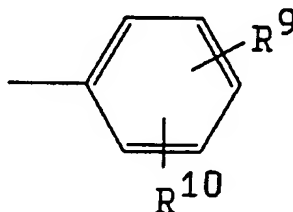


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $\text{NR}''\text{OH}$, $\text{NR}''\text{OR}'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azido-

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alkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_vW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR_2' , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR_2'$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_4OH$ or $COO(CH_2)_4OR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

30



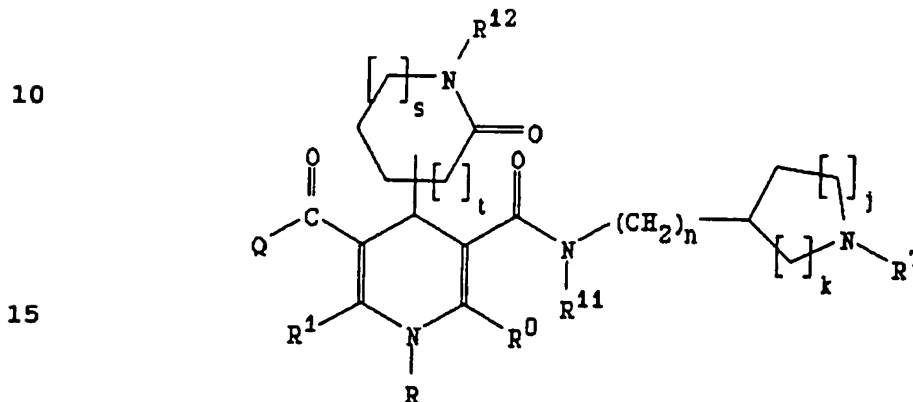
wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR_2^v , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is

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a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; wherein n is 2, 3 or 4; and wherein s and t are independently the same or different and are 0, 1, 2 or 3.

117. A compound having the structure:

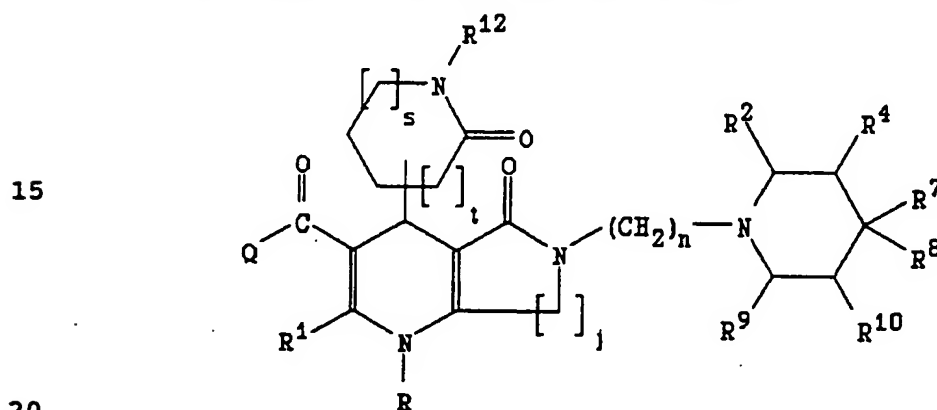


wherein Q is OH, OR'' , SH, SR''' , NH_2 , NHR''' , NR_2''' , $NR''OH$, $NR''OR'''$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R^0 and R^1 are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or $(CH_2)_tW$, where W is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 , NO_2 or $CH_2W^0(CH_2)_tW^1$, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W^0 is O, S or NH, where W^1 is NH_2 , NHR' , NR_2' , $NHOH$, $N^+R_3'Z^-$, $NHCOR'$, N_3 or NO_2 , and where R' is a linear or branched chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3,

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4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁷ is an aryl or diarylalkyl group; wherein R¹¹ is H or a linear chain alkyl group; wherein R¹² is H or a linear chain alkyl group; wherein j and k are independently the same or different and are 0, 1, 2, 3 or 4; wherein n is 2, 3 or 4; and wherein s and t are independently the same or different and are 0, 1, 2 or 3.

118. A compound having the structure:

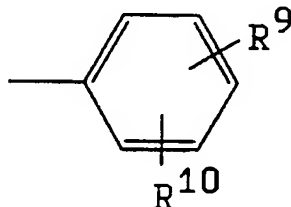


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R¹ is H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_jW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_kW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched

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chain alkyl group, or an aryl group, where Z^- is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R^2 , R^9 and R^{10} are independently the same or different and are H or a linear or branched chain alkyl group; wherein R^4 is H or a linear or branched chain alkyl, alkyloxymethyl, or alkoxyethyl group, or a hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene group, or an aryl group having the structure:

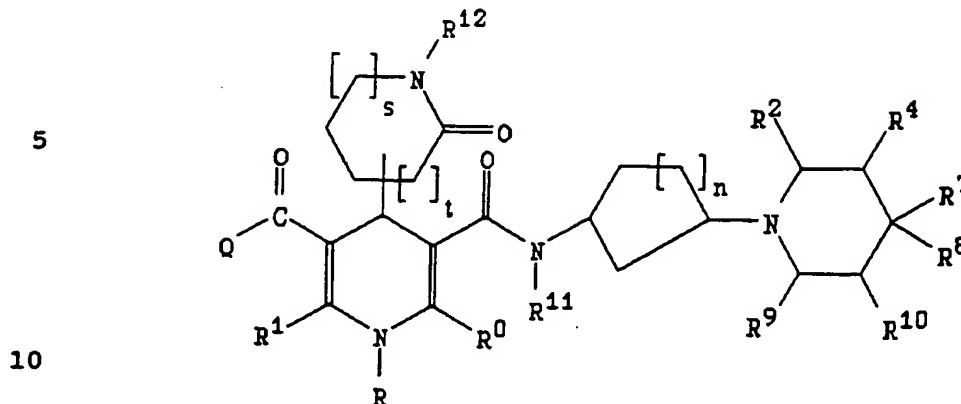
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25 wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; wherein n is 2, 3 or 4; and wherein s and t are independently the same or different and are 0, 1, 2 or 3.

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119. A compound having the structure:

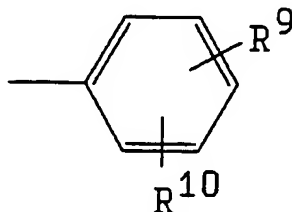


wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'',
NR''OH, NR''OR''', or a linear or branched chain alkyl
group, or an arylalkyl group, or an alkenyl or alkynyl
15 group, or an aryl group, where R'' is H, a linear or
branched chain alkyl group, trialkylsilylalkyl,
cyanoalkyl, or an aryl group, and R''' is a linear or
branched chain alkyl group, or an aryl group; wherein R⁰
and R¹ are independently the same or different and are H,
20 a linear or branched chain alkyl, an alkoxyalkyl, azido-
alkyl, aminoalkoxyalkyl, azidoalkoxyalkyl,
trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl
group, or (CH₂)_vW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻,
NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched
25 chain alkyl group, or an arylalkyl group, or an alkenyl
or alkynyl group, or an aryl group, where R' is a linear
or branched chain alkyl group, or an aryl group, where W⁰
is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻,
NHCOR', N₃ or NO₂, and where R' is a linear or branched
30 chain alkyl group, or an aryl group, where Z⁻ is a
pharmaceutically acceptable counterion, and t is 1, 2, 3,
4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H or a
linear or branched chain alkyl or acyl group, or an aryl
group; wherein R², R⁹ and R¹⁰ are independently the same or
35 different and are H or a linear or branched chain alkyl
group; wherein R⁴ is H or a linear or branched chain
alkyl, alkyloxymethyl, or alkoxyethyl group, or a

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hydroxymethyl or hydroxyethyl group, or a linear or branched chain alkenylalkyl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$,
 5 $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene
 10 group, or an aryl group having the structure:

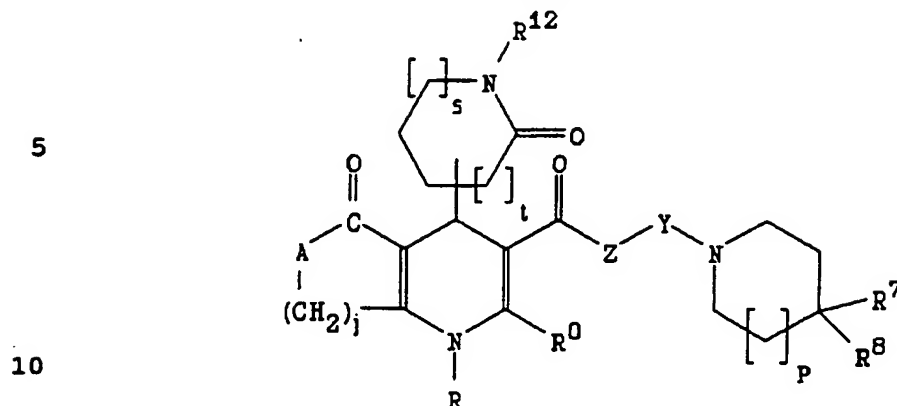
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^{iv} , $OCOR^{iv}$, $OCOOR^{iv}$, $OCONHR^{iv}$, NH_2 , NHR^{iv} , NR^{iv}_2 , $NHCOR^{iv}$, $NHCOOR^{iv}$ or $NHCONHR^{iv}$, where
 20 R' is a linear or branched chain alkyl group, and R^{iv} is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{11} is H or a linear chain alkyl group; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein n is 0, 1, 2, 3 or 4; and
 25 wherein s and t are independently the same or different and are 0, 1, 2 or 3.

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120. A compound having the structure:



wherein Q is OH, OR', SH, SR'', NH₂, NHR'', NR'OH, NR'OR'', where R' is H, or a linear or branched chain alkyl, trialkylsilylalkyl, or cyanoalkyl group, or an aryl group, and where R'' is a linear or branched chain alkyl group, or an aryl group; wherein Y is -(CH₂)_n-, where n is 1, 2, 3, 4 or 5; -(CH₂)_h-O-(CH₂)_k-, where h and k are independently the same or different and are 2, 3 or 4; -(CH₂)_h-CH=CH-(CH₂)_k-; or -(CH₂)_h-C≡C-(CH₂)_k-, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein A is CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Z is O, NH, NCHO, NCOR^b, NR^b, NOR^b, or CH₂, where R^b is a methyl, ethyl or propyl group; wherein R is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein R⁰ is H, or a linear or branched chain alkyl, alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, or hydroxyalkyl group, or an aryl group; wherein R⁷ and R⁸ are independently the same or different and are H, CN, CF₃, OH, OR', OCOR', NH₂, NHR', NR'₂, NHCOR', CONH₂, CONHR', CONR'₂, COOH, COOR', CHO, COR', COSH, COSR', COO(CH₂)₄OH or COO(CH₂)₄OR', or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or

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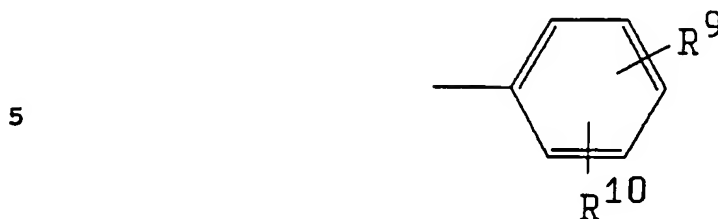
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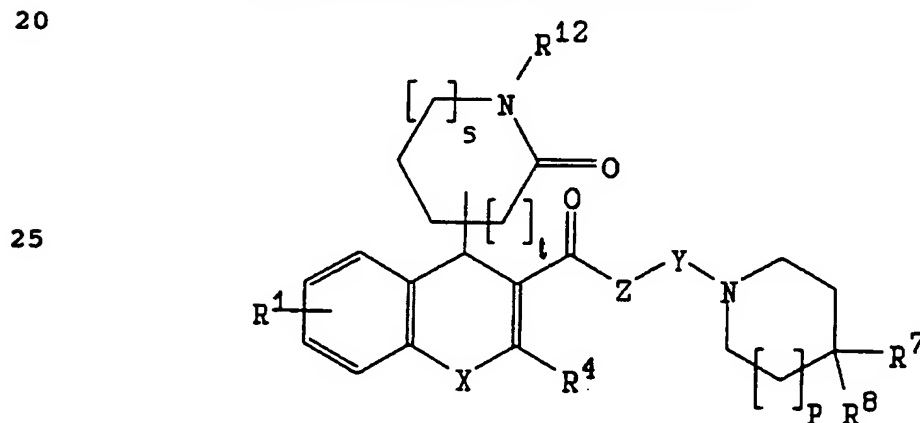
thiophene group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where R^v is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein p is 0, 1, 2 or 3; and

15 wherein s and t are independently the same or different and are 0, 1, 2 or 3.

121. A compound having the structure:



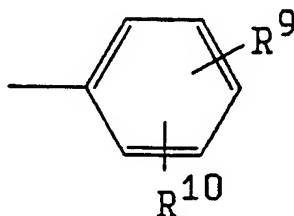
30 wherein X is NH, NR, O or S, where R is H or a linear or branched chain alkyl or acyl group, or an aryl group; Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-$

35 $(\text{CH}_2)_k-$, where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or

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propyl group; wherein R^1 is H, Cl, Br, I, F, NO_2 , CN, OH, OR'' , OCOR'' , NH_2 , NR'' , NHCOR'' or CF_3 , where R'' is a linear or branched chain alkyl group, or an aryl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_q\text{OH}$ or $\text{COO}(\text{CH}_2)_q\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:

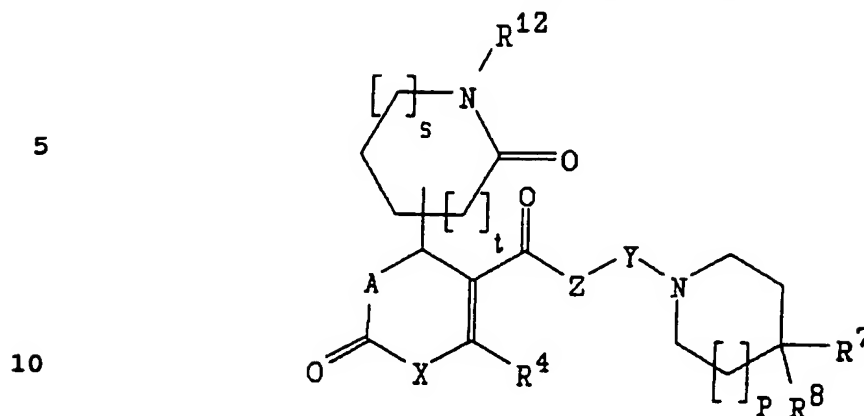
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wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR^v_2 , NHCOR^v , NHCOOR^v or NHCONHR^v , where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein p is 0, 1, 2 or 3; and wherein s and t are independently the same or different and are 0, 1, 2 or 3.

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122. A compound having the structure:



wherein A is CH_2 , CR_2 , NH , NR , NCHO , NCOR , NOH , O or S , where R is a methyl, ethyl or propyl group; wherein X is

15 NH , NR' , O or S , where R' is H or a linear or branched chain alkyl or acyl group, or an aryl group; wherein Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$,

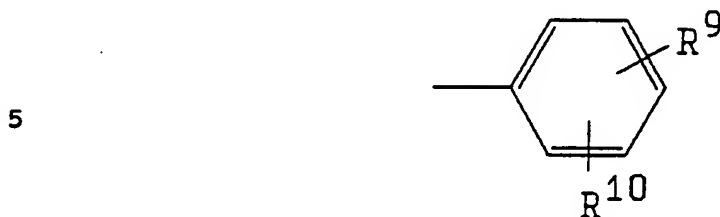
20 where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O , NH , NCHO , NCOR'' , NR'' , NOR'' or CH_2 , where R'' is a methyl, ethyl or propyl group; wherein R^4 is H, or a linear or branched chain alkyl group, or an aryl group; wherein R^7 and R^8 are

25 independently the same or different and are H, CN , CF_3 , OH , OR' , OCOR' , NH_2 , NHR' , NR'_2 , NHCOR' , CONH_2 , CONHR' , CONR'_2 , COOH , COOR' , CHO , COR' , COSH , COSR' , $\text{COO}(\text{CH}_2)_4\text{OH}$ or $\text{COO}(\text{CH}_2)_4\text{OR}'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl

30 group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrol, furyl or thiophene

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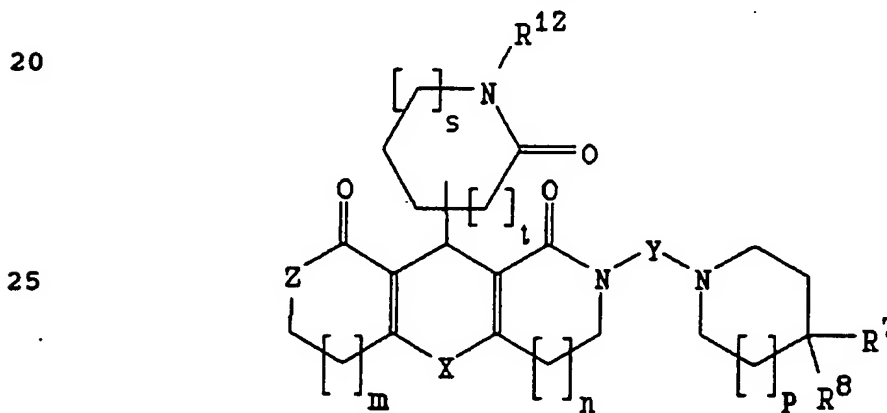
group, or an aryl group having the structure:



wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , OCOR^v , OCOOR^v , OCONHR^v , NH_2 , NHR^v , NR^v , NHCOR^v , NHCOOR^v or NHCONHR^v , where R^v is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein p is 0, 1, 2 or 3; and

15 wherein s and t are independently the same or different and are 0, 1, 2 or 3.

123. A compound having the structure:

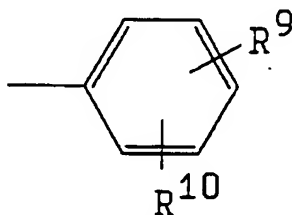


30 wherein X is NH, NR, O or S, where R is H or a linear or branched chain alkyl or acyl group, or an aryl group; Y is $-(\text{CH}_2)_n-$, where n is 1, 2, 3, 4 or 5; $-(\text{CH}_2)_h-\text{O}-(\text{CH}_2)_k-$, where h and k are independently the same or different and are 2, 3 or 4; $-(\text{CH}_2)_h-\text{CH}=\text{CH}-(\text{CH}_2)_k-$; or $-(\text{CH}_2)_h-\text{C}\equiv\text{C}-(\text{CH}_2)_k-$,

35 where h and k are independently the same or different and are 1, 2, 3 or 4; wherein Z is O, NH, NCHO, NCOR' , NR' , NOR' or CH_2 , where R' is a methyl, ethyl or propyl group;

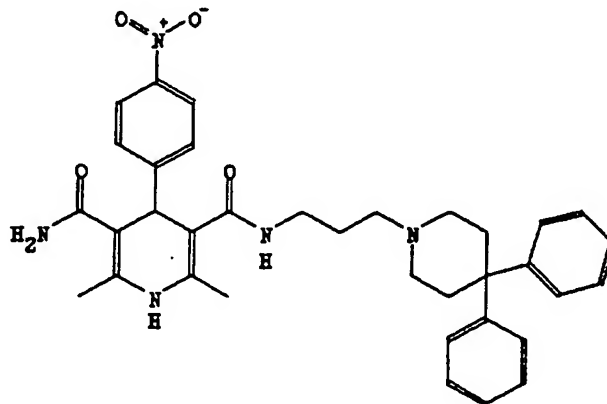
-728-

wherein R^7 and R^8 are independently the same or different and are H, CN, CF_3 , OH, OR' , $OCOR'$, NH_2 , NHR' , NR'_2 , $NHCOR'$, $CONH_2$, $CONHR'$, $CONR'_2$, $COOH$, $COOR'$, CHO , COR' , $COSH$, $COSR'$, $COO(CH_2)_qOH$ or $COO(CH_2)_qOR'$, or a benzyl group, a linear or branched chain alkyl or cycloalkyl group, or are a heteroaryl group comprising a pyridyl, indolyl, indolylalkyl, quinolinyl, isoquinolinyl, pyrrolyl, furyl or thiophene group, or an aryl group having the structure:



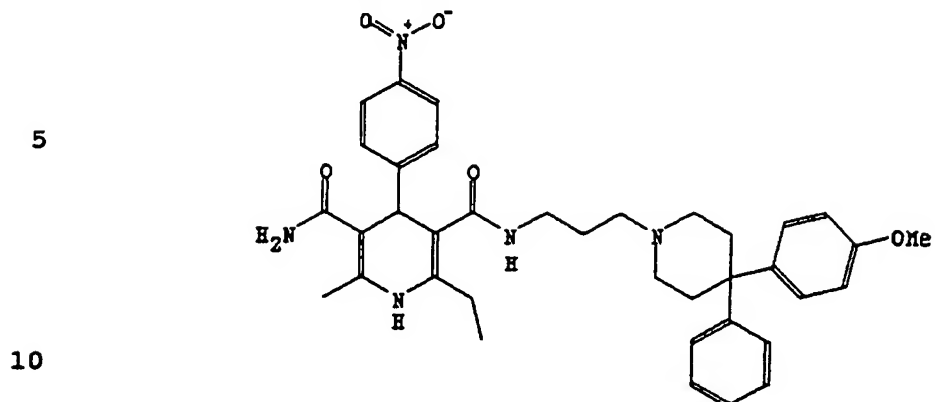
wherein R^9 and R^{10} are independently the same or different and are H, Cl, Br, I, F, OH, NO_2 , N_3 , OR^v , $OCOR^v$, $OCOOR^v$, $OCONHR^v$, NH_2 , NHR^v , NR^v_2 , $NHCOR^v$, $NHCOOR^v$ or $NHCONHR^v$, where R' is a linear or branched chain alkyl group, and R^v is a linear or branched chain alkyl group, and q is 2, 3, 4 or 5; wherein R^{12} is H or a linear chain alkyl group; wherein j is 1, 2, 3 or 4; wherein m and n are independently the same or different and are 0 or 1; wherein p is 0, 1, 2 or 3; and wherein s and t are independently the same or different and are 0, 1, 2 or 3.

124. The compound of claim 30 having the structure:

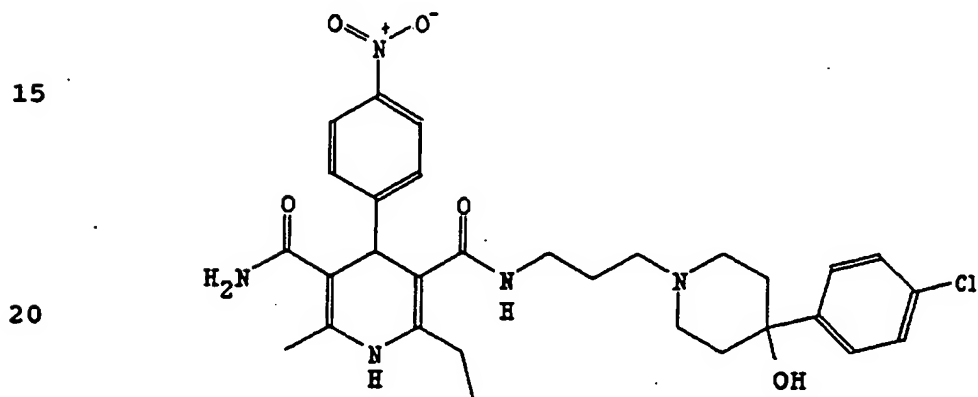


-729-

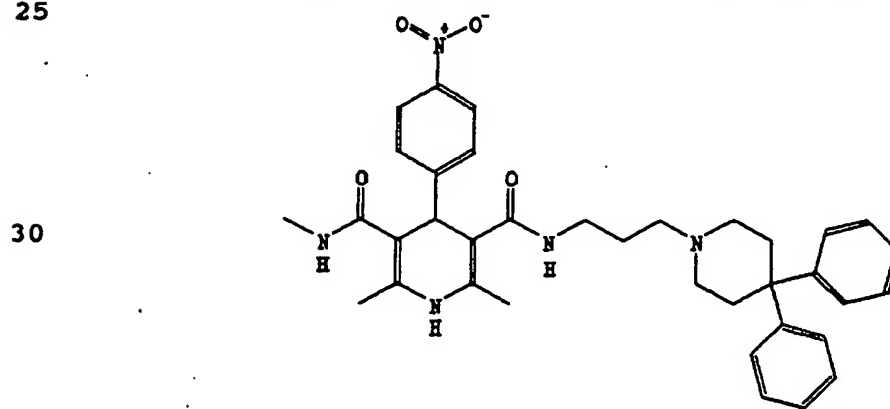
125. The compound of claim 30 having the structure:



126. The compound of claim 30 having the structure:



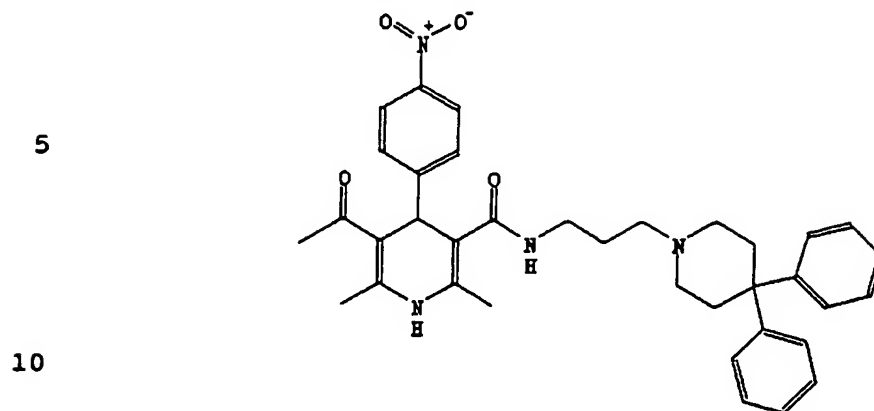
127. The compound of claim 30 having the structure:



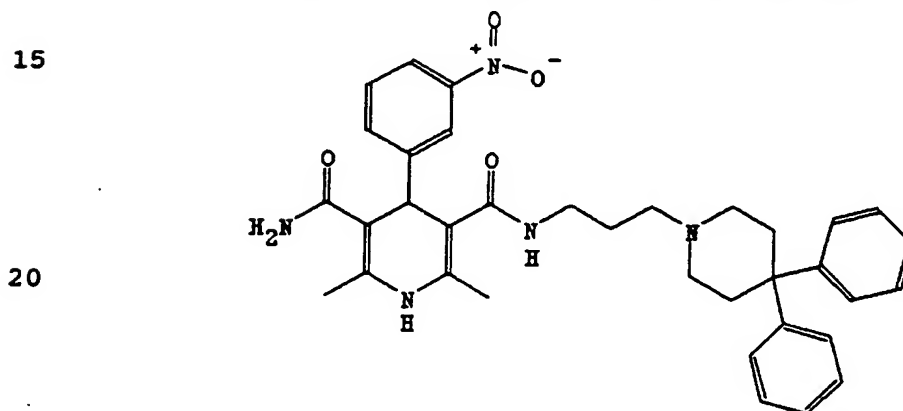
35

-730-

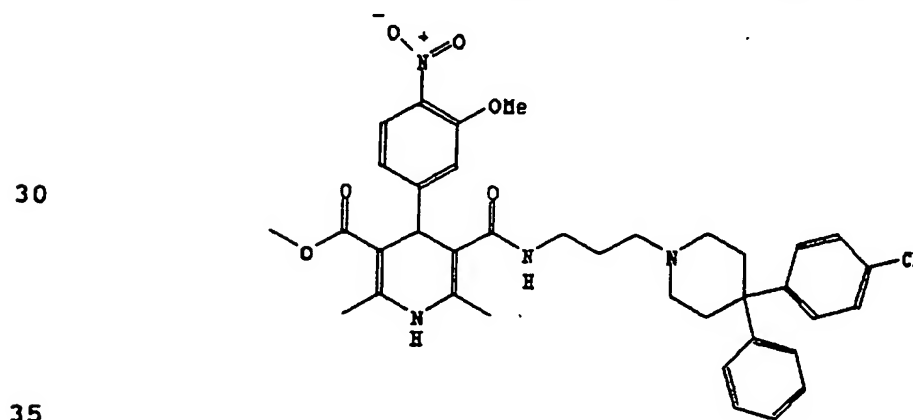
128. The compound of claim 30 having the structure:



129. The compound of claim 30 having the structure:

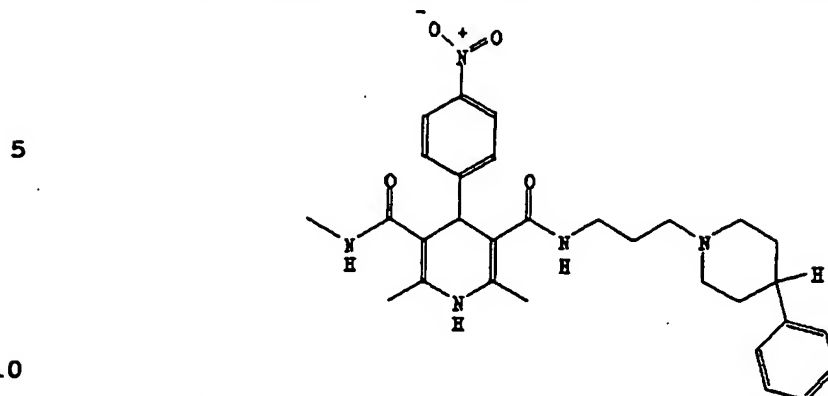


130. The compound of claim 30 having the structure:

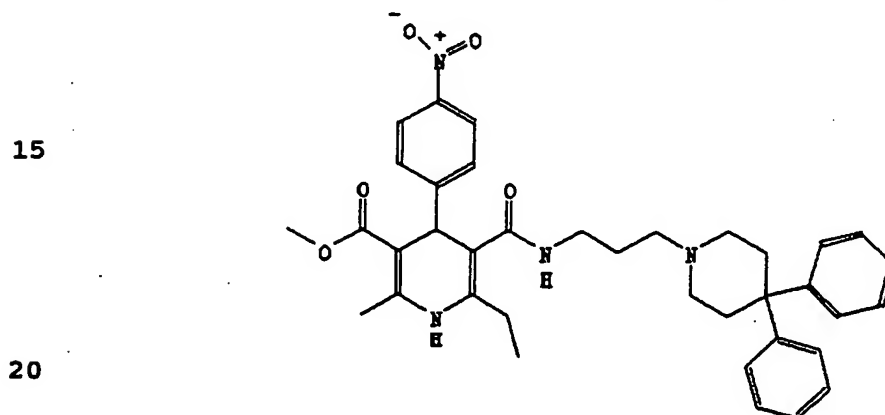


-731-

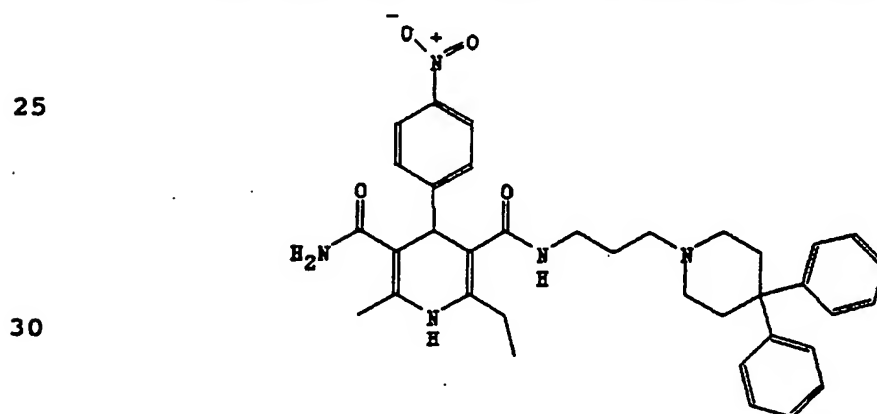
131. The compound of claim 30 having the structure:



132. The compound of claim 30 having the structure:

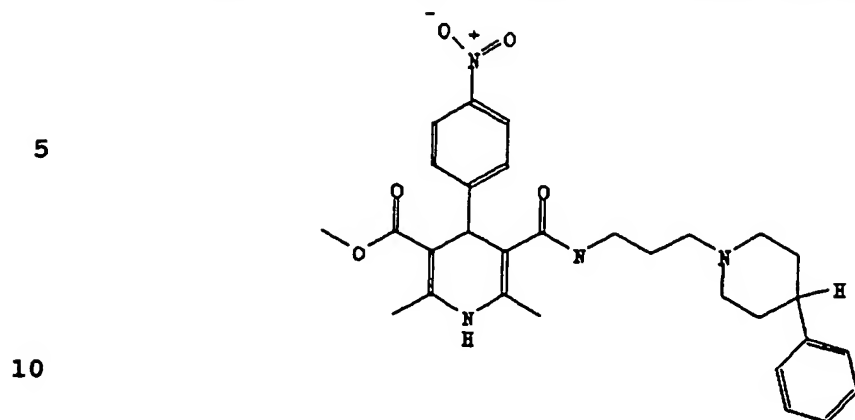


133. The compound of claim 30 having the structure:

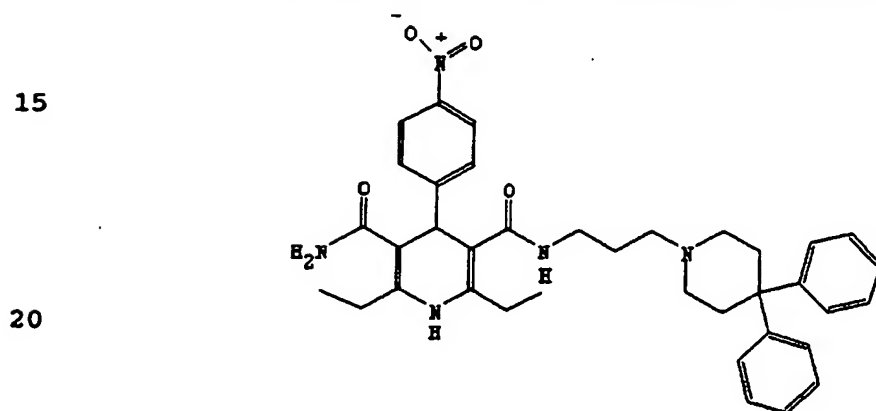


-732-

134. The compound of claim 30 having the structure:

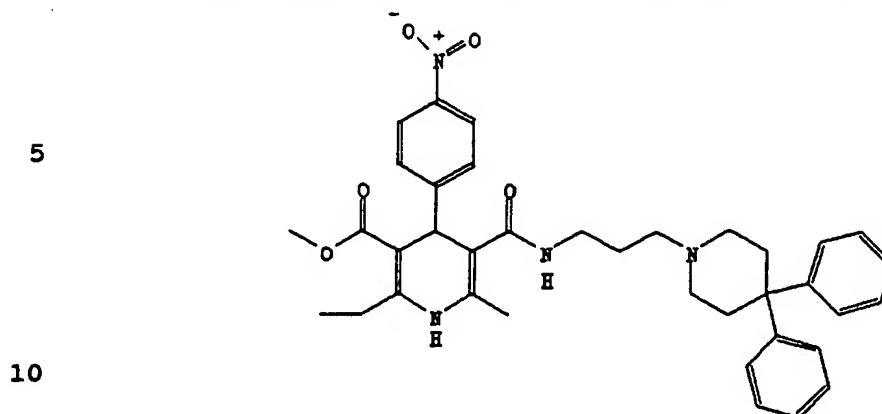


135. The compound of claim 30 having the structure:

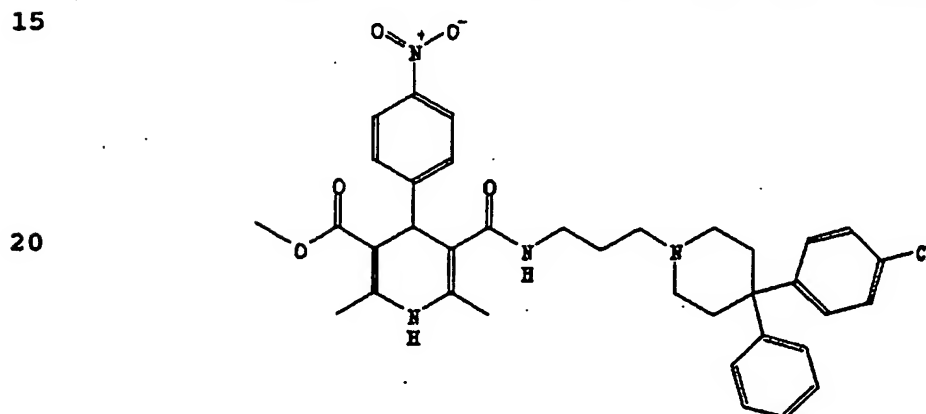


-733-

136. The compound of claim 30 having the structure:



137. The compound of claim 30 having the structure:



25

138. A method of treating benign prostatic hyperplasia in a subject which comprises administering to the subject a therapeutically effective amount of any one of the compounds of claims 124 to 137.

30

139. A method of lowering intraocular pressure in a subject which comprises administering to the subject a therapeutically effective amount of any one of the compounds of claims 124 to 137.

35

140. A method of inhibiting cholesterol synthesis in a subject which comprises administering to the subject a

-734-

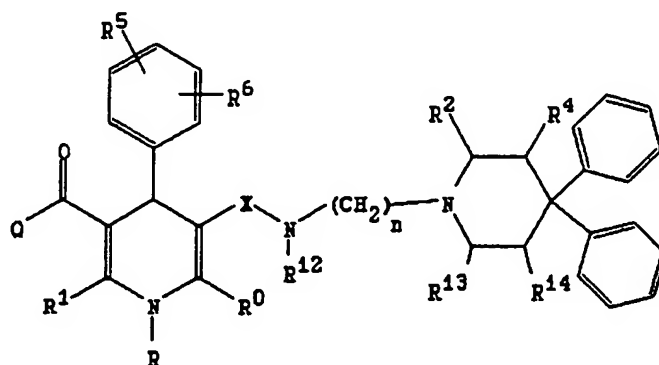
therapeutically effective amount of any one of the compounds of claims 124 to 137.

141. A method of treating diseases mediated by α_1 receptors in a subject which comprises administering to the subject a therapeutically effective amount of any one of the compounds of claims 124 to 137.

142. The compound of claim 30 having the structure:

10

15



wherein X is C=O, CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_nW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_mW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or

-735-

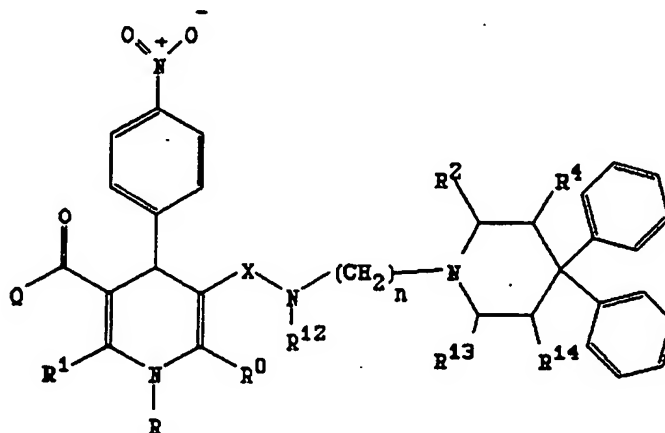
NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z' is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R², R¹³, and R¹⁴ are independently the same or different and are H, or a linear or branched chain alkyl, hydroxyalkyl, alkoxyalkyl, amino alkyl or aryl group; wherein R⁴ is a linear or branched chain alkyl, alkoxyalkyl, hydroxyalkyl or a linear or branched chain alkenylalkyl group; wherein R⁵ and R⁶ are independently the same or different and are H, OH, Cl, Br, I, F, NO₂, CN, N₃, NH₂, CF₃, a linear or branched chain alkyl, alkoxy, alkoxy carbonyl, acyl, alkylsulfoxide, alkylsulfoxide, or mono- or dialkylamino group, or together constitute a methylenedioxy group; wherein R¹² is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

143. The compound of claim 142 having the structure:

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30

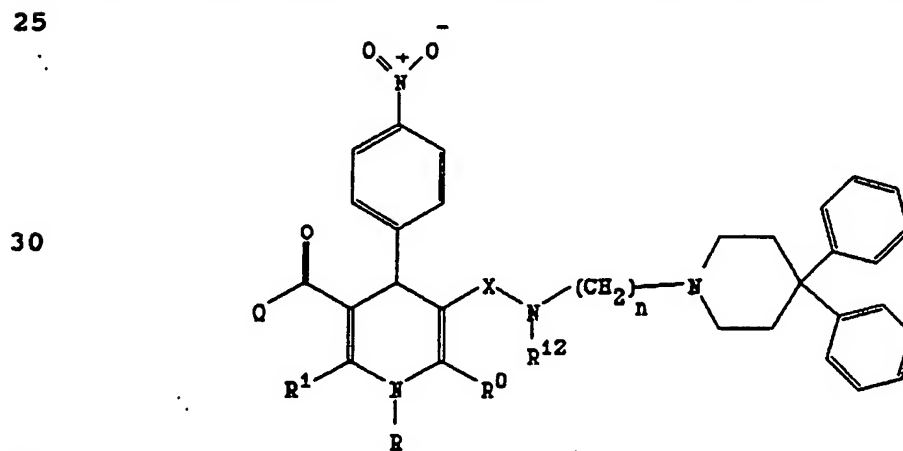


wherein X is C=O, CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Q is OH, OR'', SH, SR'', NH₂, NHR'', NR'', NR''OH, NR''OR'', or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl, or an aryl

-736-

group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂, or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R², R¹³, and R¹⁴ are independently the same or different and are H, or a linear or branched chain alkyl, hydroxyalkyl, alkoxyalkyl, amino alkyl or aryl group; wherein R⁴ is a linear or branched chain alkyl, alkoxyalkyl, hydroxyalkyl or a linear or branched chain alkenylalkyl group; wherein R¹² is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

144. The compound of claim 143 having the structure:



wherein X is C=O, CH₂, CR^a, NH, NR^a, NCHO, NCOR^a, NOH, O or S, where R^a is a methyl, ethyl or propyl group; wherein Q

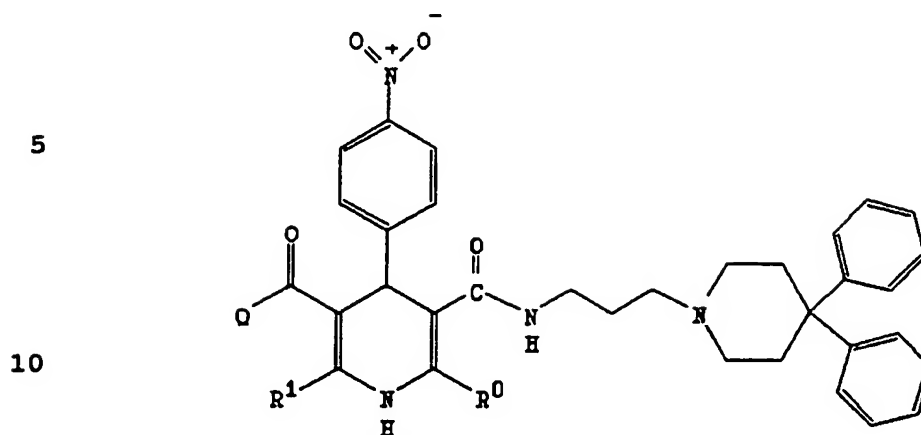
-737-

is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl, or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group; wherein R¹² is H or a linear chain alkyl group; and wherein n is 2, 3 or 4.

25 2

-738-

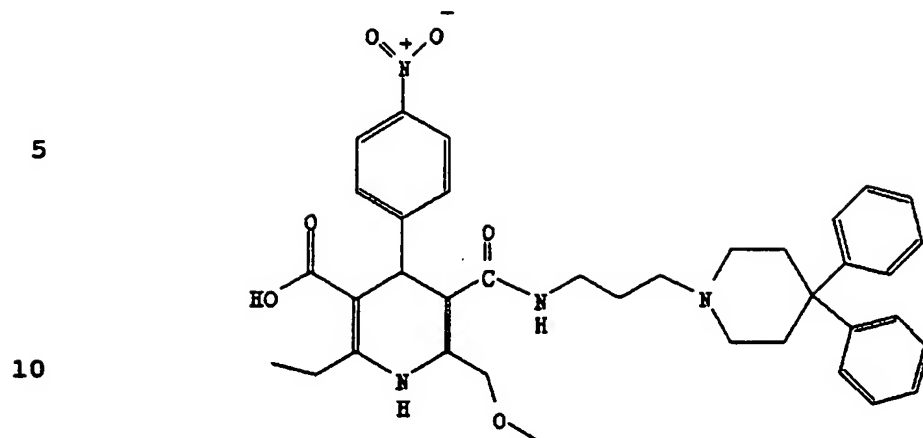
145. The compound of claim 144 having the structure:



wherein Q is OH, OR'', SH, SR''', NH₂, NHR''', NR₂'', NR''OH, NR''OR''' or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R'' is H, a linear or branched chain alkyl group, trialkylsilylalkyl, cyanoalkyl or an aryl group, and R''' is a linear or branched chain alkyl group, or an aryl group; wherein R⁰ and R¹ are independently the same or different and are H, a linear or branched chain alkyl, an alkoxyalkyl, azidoalkyl, aminoalkoxyalkyl, azidoalkoxyalkyl, trihaloalkoxyalkyl, aminoalkyl, hydroxyalkyl or an aryl group, or (CH₂)_tW, where W is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃, NO₂ or CH₂W⁰(CH₂)_vW¹, or a linear or branched chain alkyl group, or an arylalkyl group, or an alkenyl or alkynyl group, or an aryl group, where R' is a linear or branched chain alkyl group, or an aryl group, where W⁰ is O, S or NH, where W¹ is NH₂, NHR', NR₂', NHOH, N⁺R₃'Z⁻, NHCOR', N₃ or NO₂, and where R' is a linear or branched chain alkyl group, or an aryl group, where Z⁻ is a pharmaceutically acceptable counterion, and t is 1, 2, 3, 4, 5 or 6 and v is 2, 3, 4, 5 or 6; and wherein R is H, a linear or branched chain alkyl or acyl group, or an aryl group.

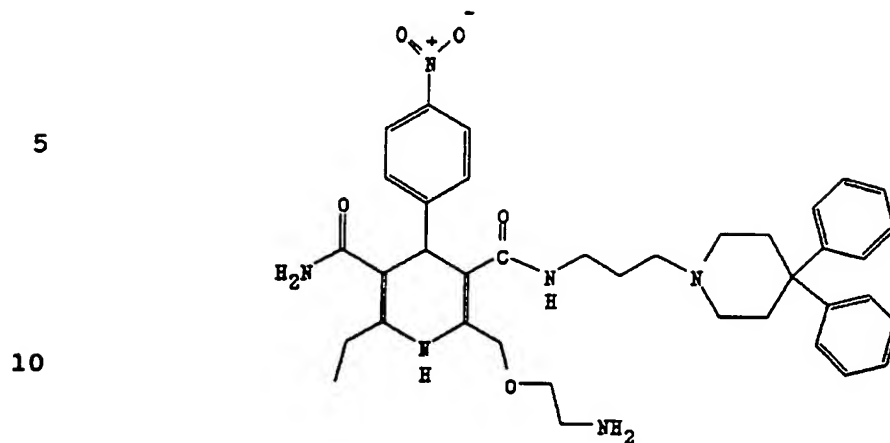
-739-

146. The compound of claim 145 having the structure:

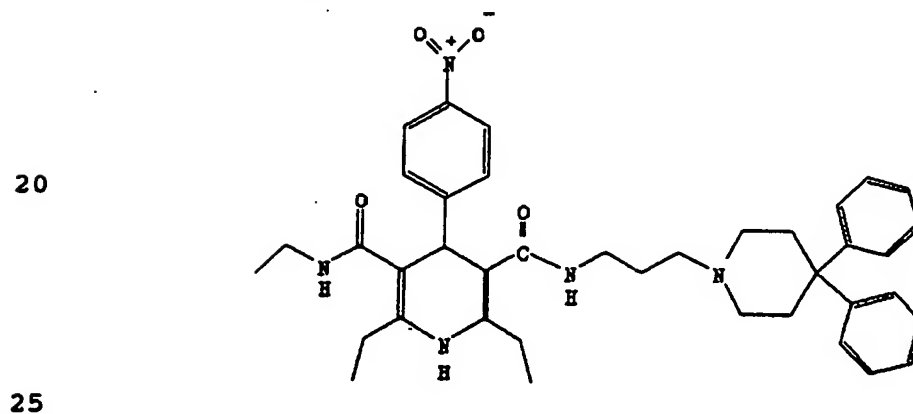


-740-

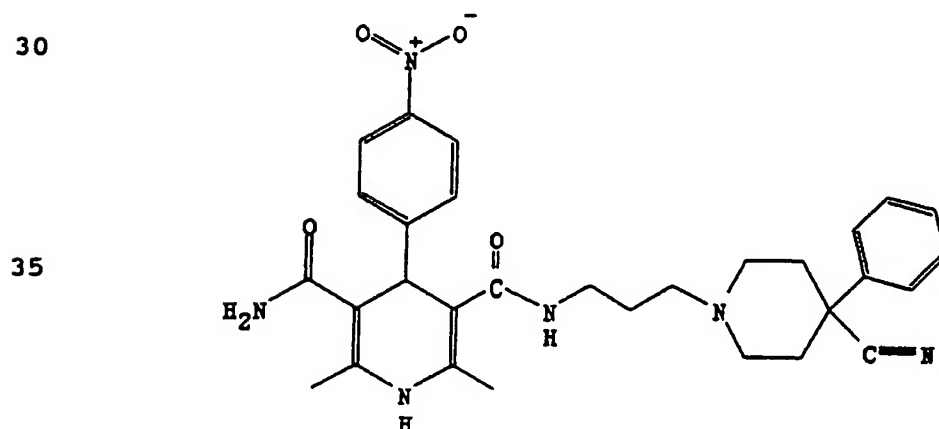
147. The compound of claim 145 having the structure:



15 148. The compound of claim 145 having the structure:



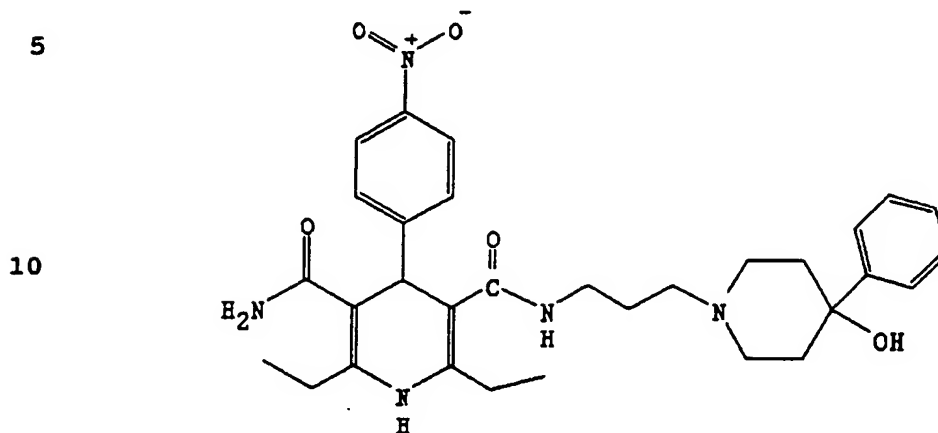
149. The (+) and (-) enantiomer of the compound of claim 31 having the structure:



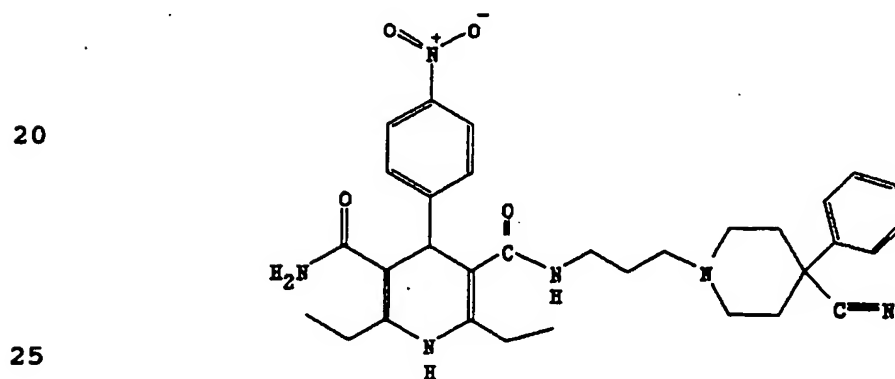
-741-

and pharmaceutically acceptable salts thereof.

150. The compound of claim 31 having the structure:



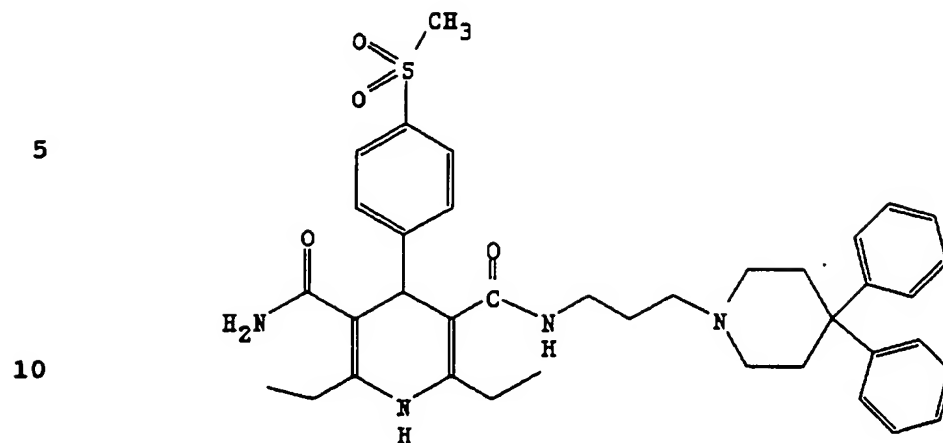
15 151. The (+) and (-) enantiomer of the compound of claim 31 having the structure:



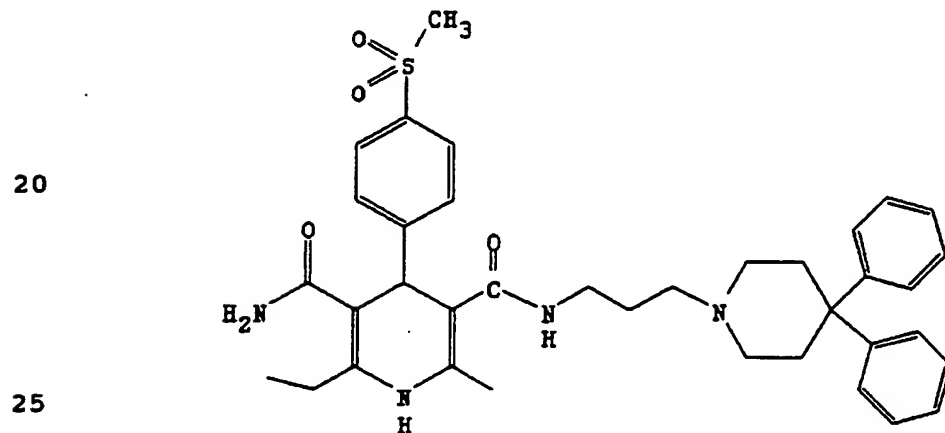
and pharmaceutically acceptable salts thereof.

-742-

152. The compound of claim 31 having the structure:

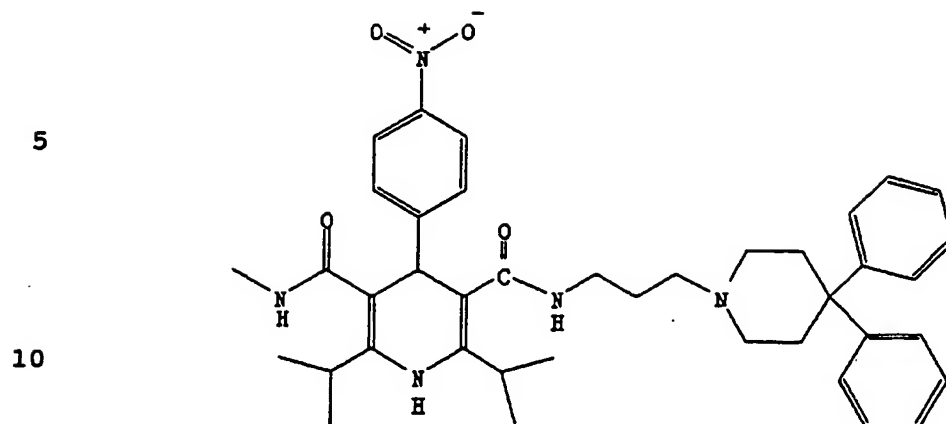


15 153. The compound of claim 31 having the structure:

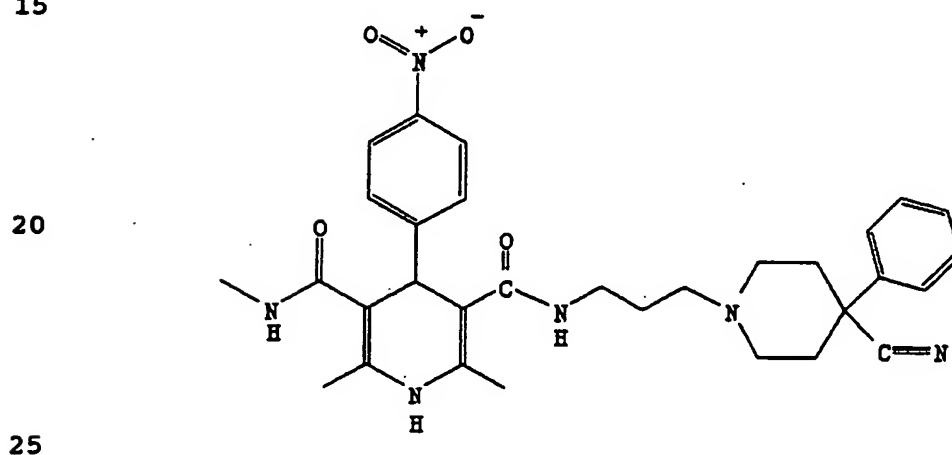


-743-

154. The compound of claim 31 having the structure:

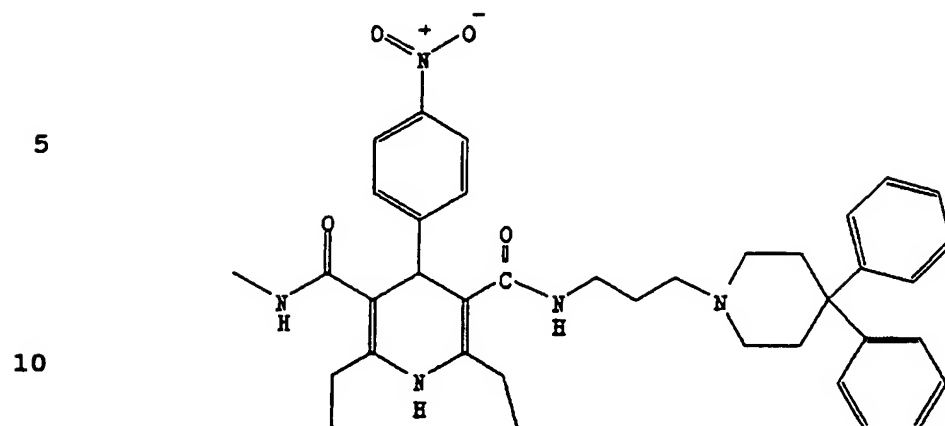


155. The compound of claim 31 having the structure:

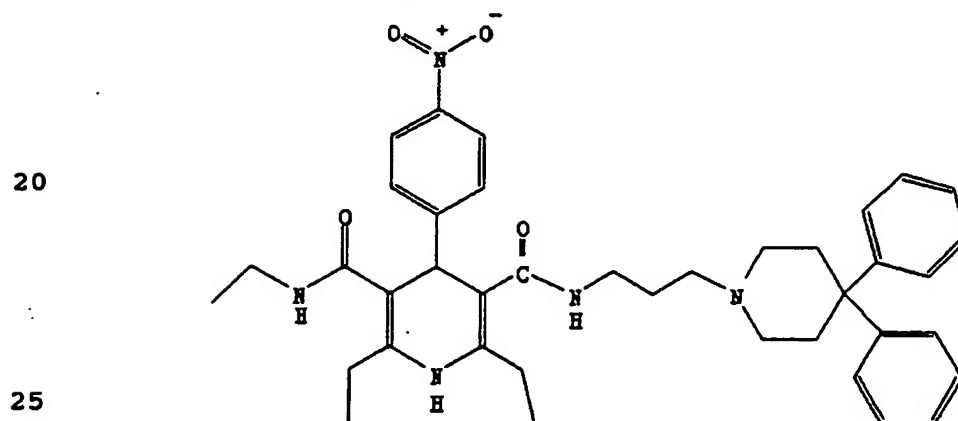


-744-

156. The compound of claim 31 having the structure:

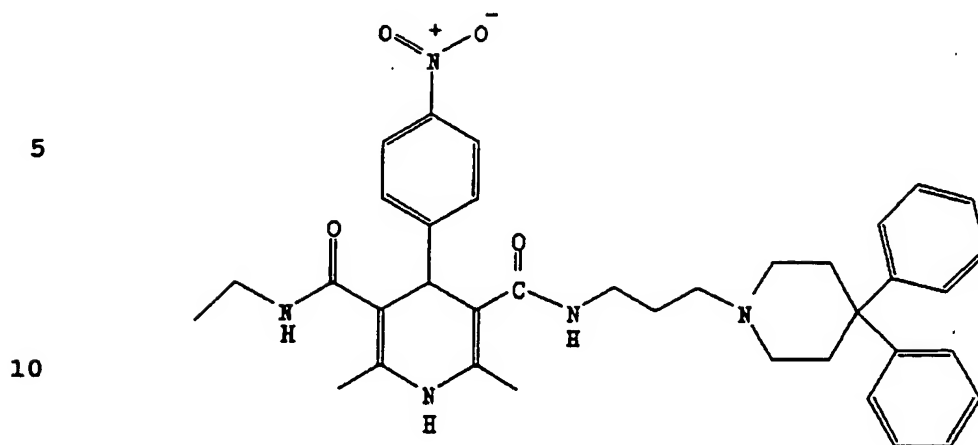


15 157. The compound of claim 31 having the structure:

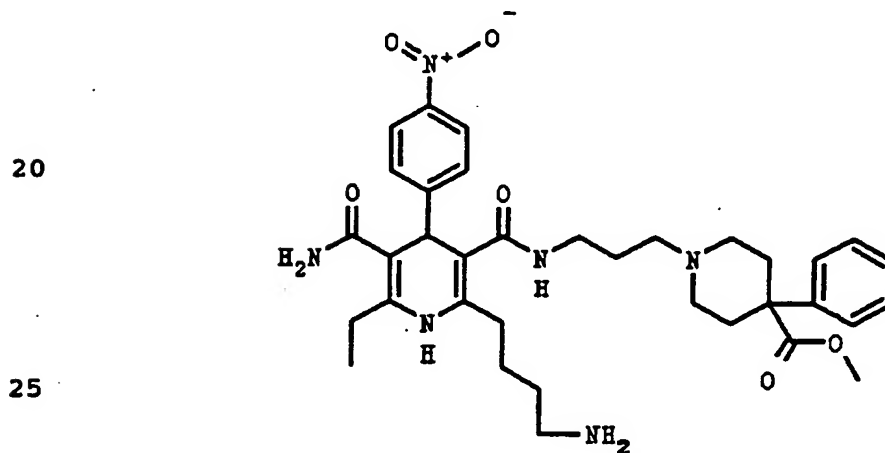


-745-

158. The compound of claim 31 having the structure:

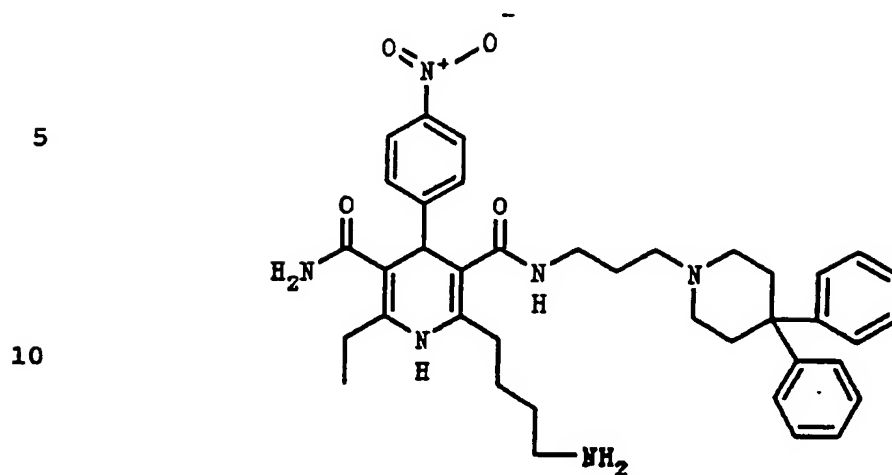


15 159. The compound of claim 31 having the structure:

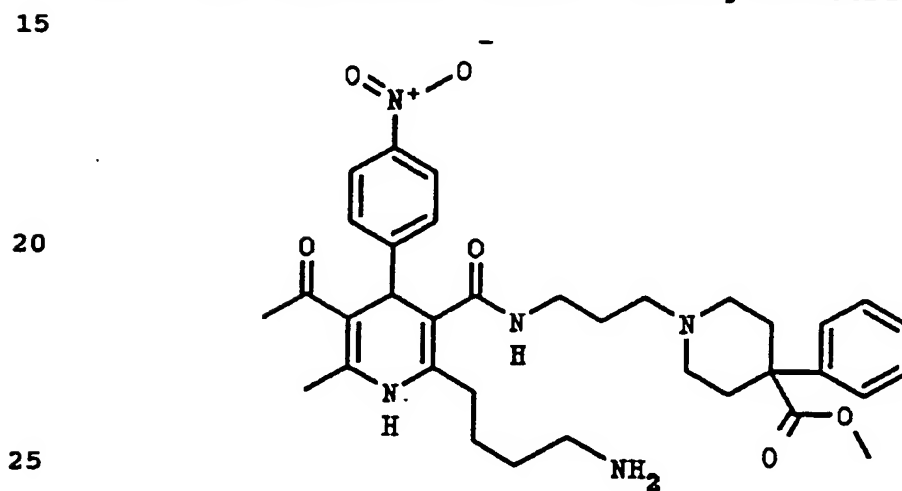


-746-

160. The compound of claim 31 having the structure:

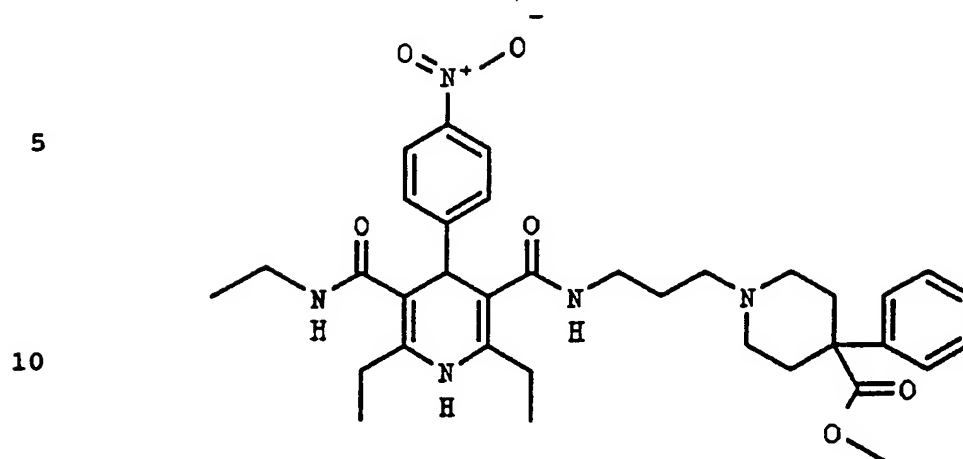


161. The compound of claim 31 having the structure:

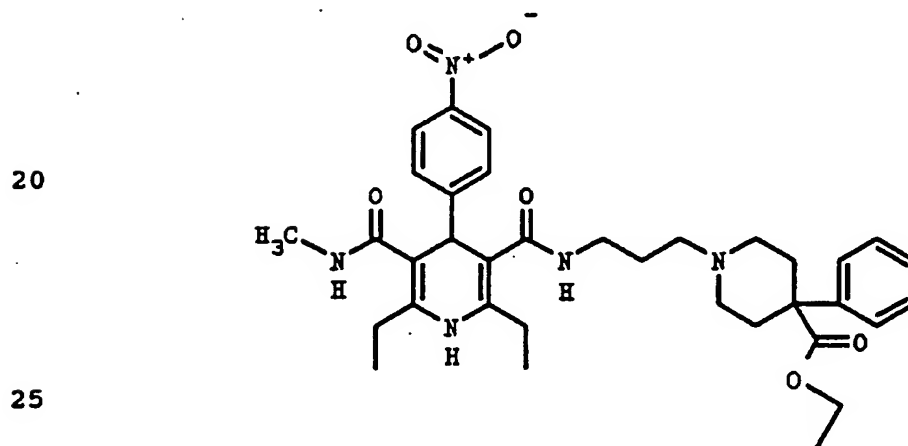


-747-

162. The compound of claim 31 having the structure:

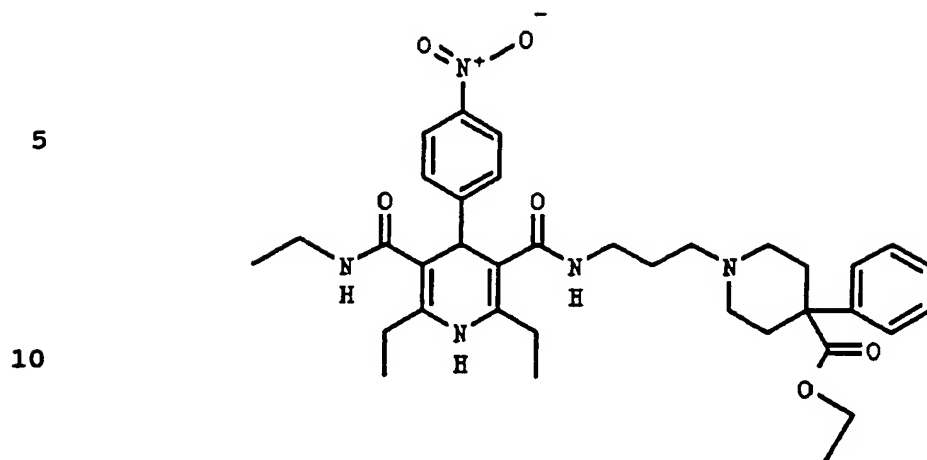


15 163. The compound of claim 31 having the structure:

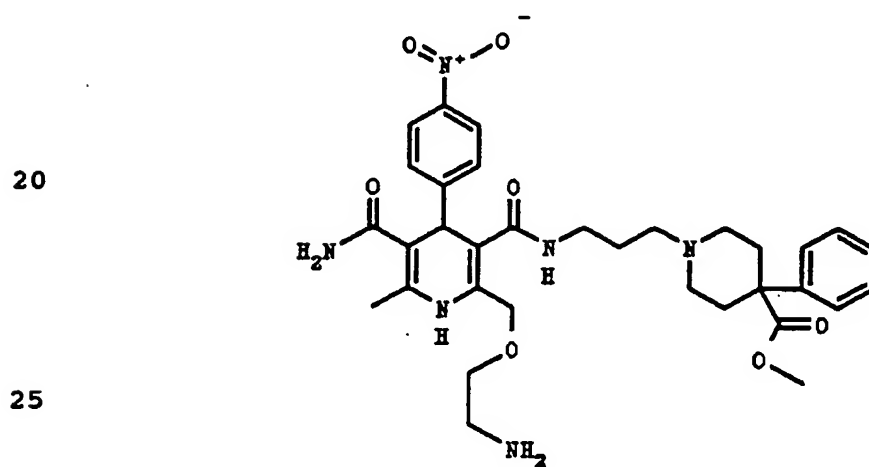


-748-

164. The compound of claim 31 having the structure:

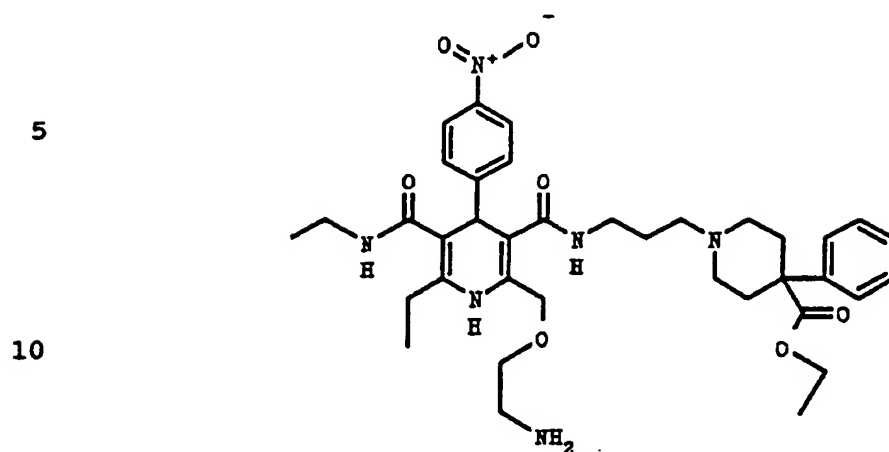


15 165. The compound of claim 31 having the structure:

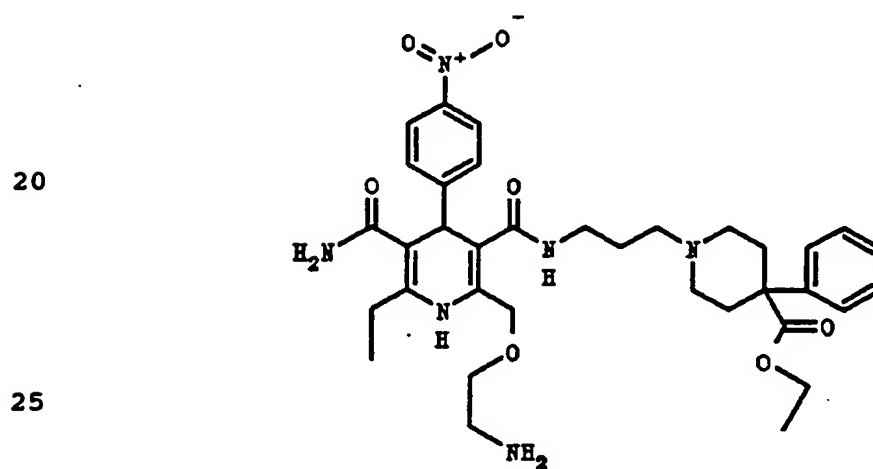


-749-

166. The compound of claim 31 having the structure:

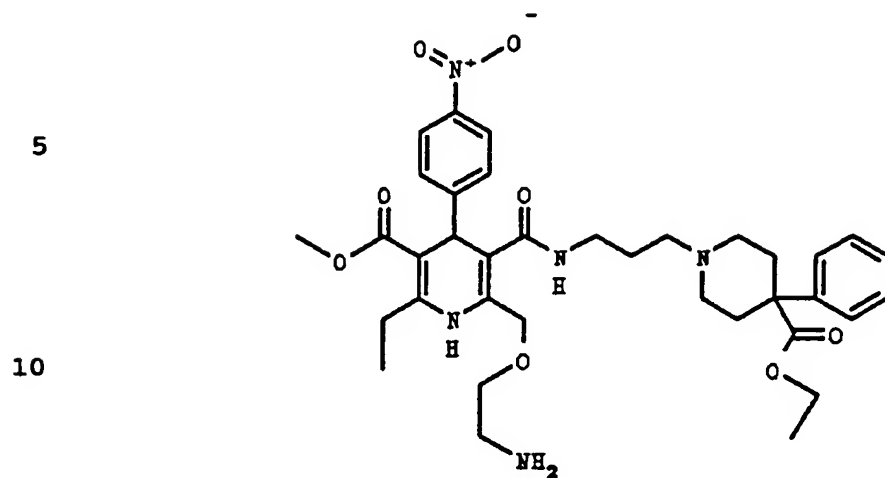


15 167. The compound of claim 31 having the structure:

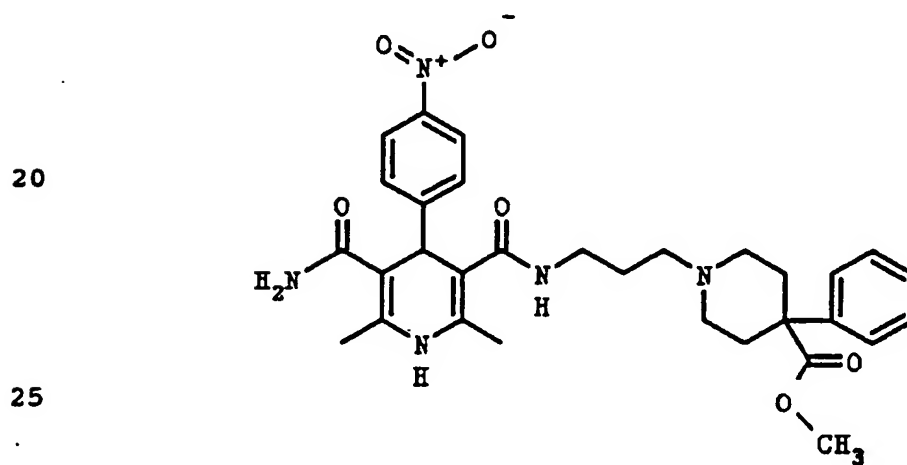


-750-

168. The compound of claim 31 having the structure:

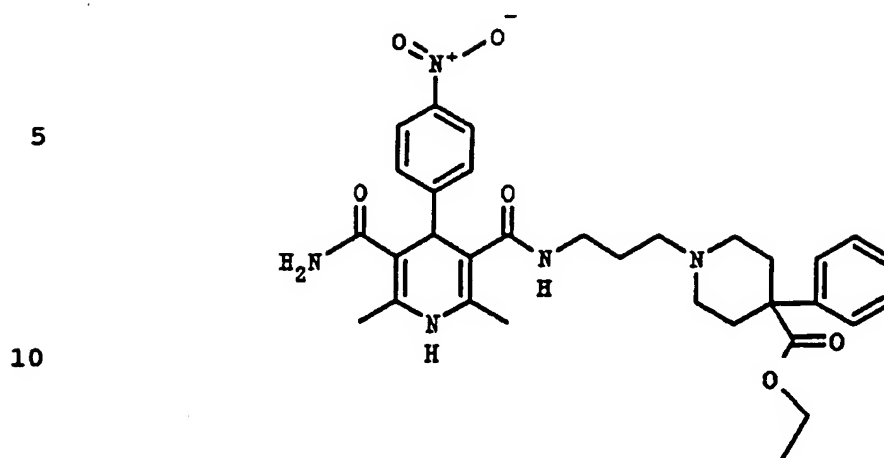


15 169. The compound of claim 31 having the structure:

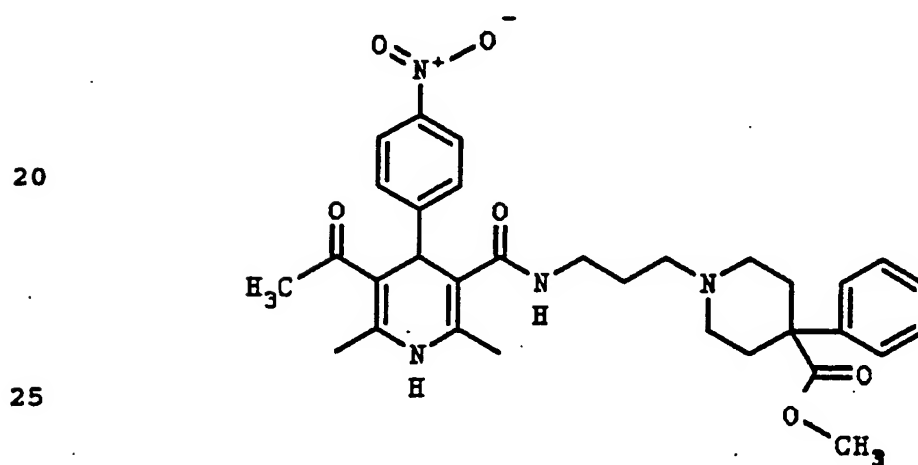


-751-

170. The compound of claim 31 having the structure:

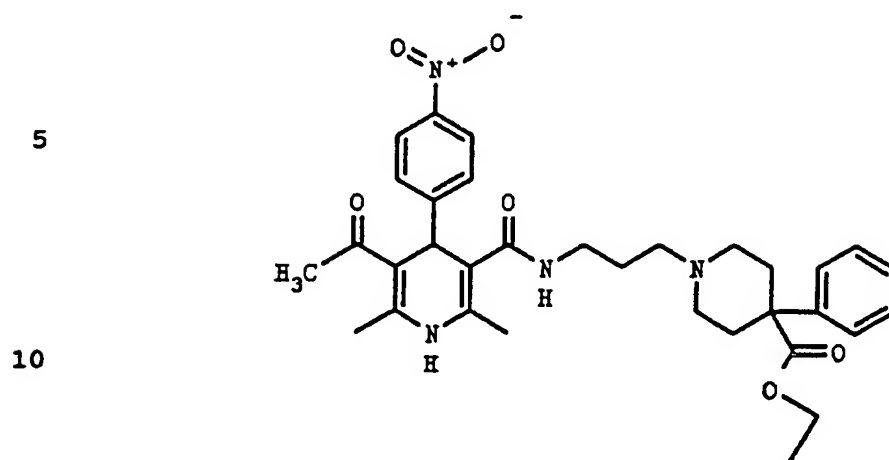


15 171. The compound of claim 31 having the structure:

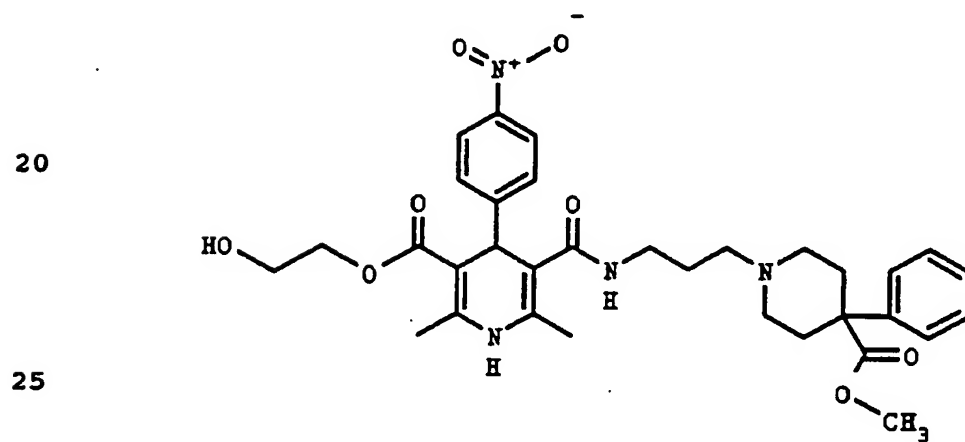


-752-

172. The compound of claim 31 having the structure:

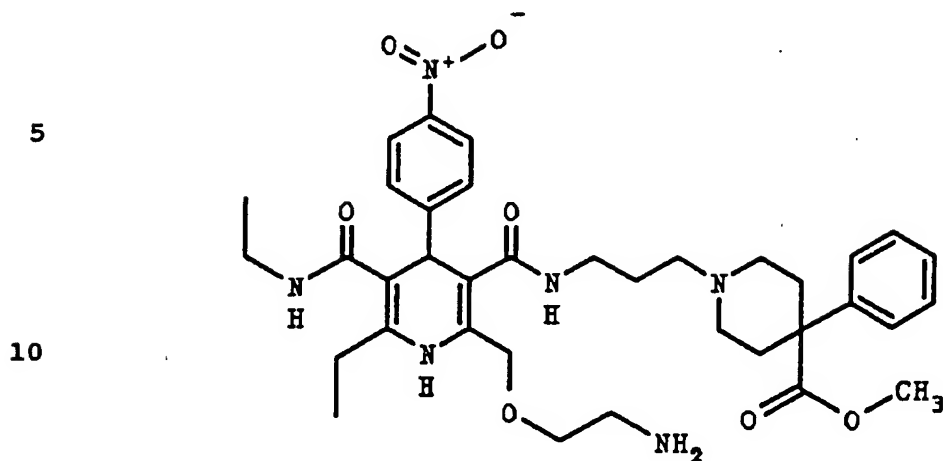


15 173. The compound of claim 31 having the structure:

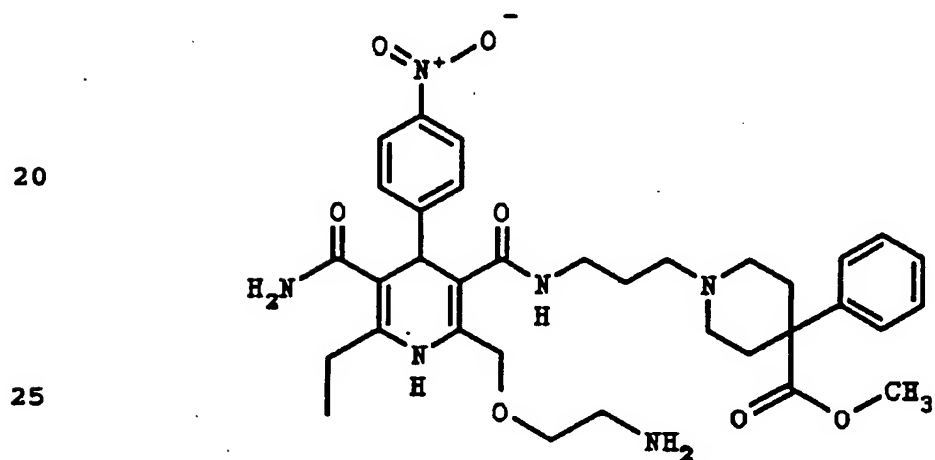


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174. The compound of claim 31 having the structure:



15 175. The compound of claim 31 having the structure:



176. A pharmaceutical composition which comprises the
30 compound of claim 30 in a therapeutically effective
amount and a pharmaceutically acceptable carrier.

177. The pharmaceutical composition of claim 176 wherein
the carrier is a solid and the composition is a tablet.

35

178. The pharmaceutical composition of claim 177 wherein
the therapeutically effective amount is an amount from

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about 0.1 to about 500 mg.

179. The pharmaceutical composition of claim 178 wherein the therapeutically effective amount is from about 1 to
5 60 mg.

180. The pharmaceutical composition of claim 177, wherein the carrier is a liquid and the composition is a solution.

10

181. The pharmaceutical composition of claim 180 wherein the therapeutically effective amount is an amount from about 0.1 to about 500 mg per mL of solution.

15 182. The pharmaceutical composition of claim 181 wherein the therapeutically effective amount is an amount from about 1 to about 60 mg per mL of solution.

20 183. The pharmaceutical composition of claim 177, wherein the carrier is a gel and the composition is a suppository.

184. The pharmaceutical composition of claim 183,
25 wherein the therapeutically effective amount is an amount from about 0.1 to about 500 mg.

185. A method of treating benign prostatic hyperplasia in a subject which comprises administering to the subject
30 a therapeutically effective amount of any one of the compounds of claim 30.

186. A method of lowering intraocular pressure in a subject which comprises administering to the subject a
35 therapeutically effective amount of any one of the compounds of claim 30.

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187. A method of inhibiting cholesterol synthesis in a subject which comprises administering to the subject a therapeutically effective amount of any one of the compounds of claim 30.

5

188. A method of treating diseases mediated by α_1 receptors in a subject which comprises administering to the subject a therapeutically effective amount of any one of the compounds of claim 30.

10

Reaction Scheme 1 (Method A)

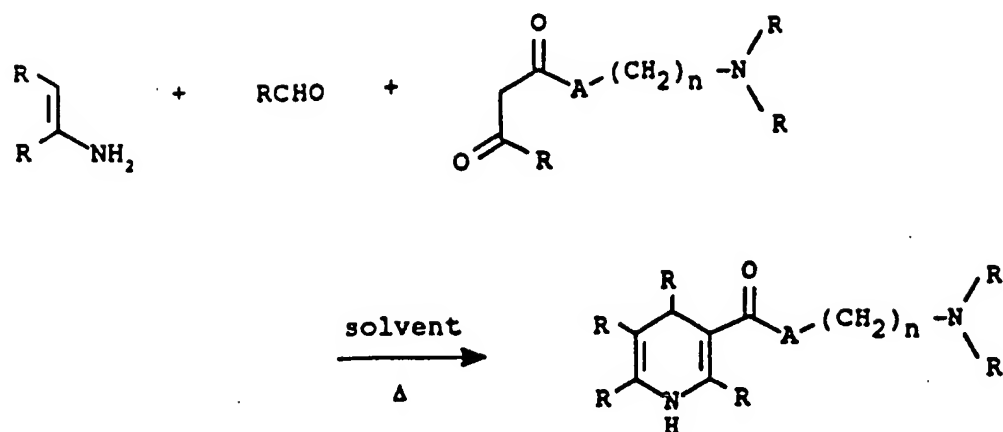


Figure 1

Reaction Scheme 2 (Method B)

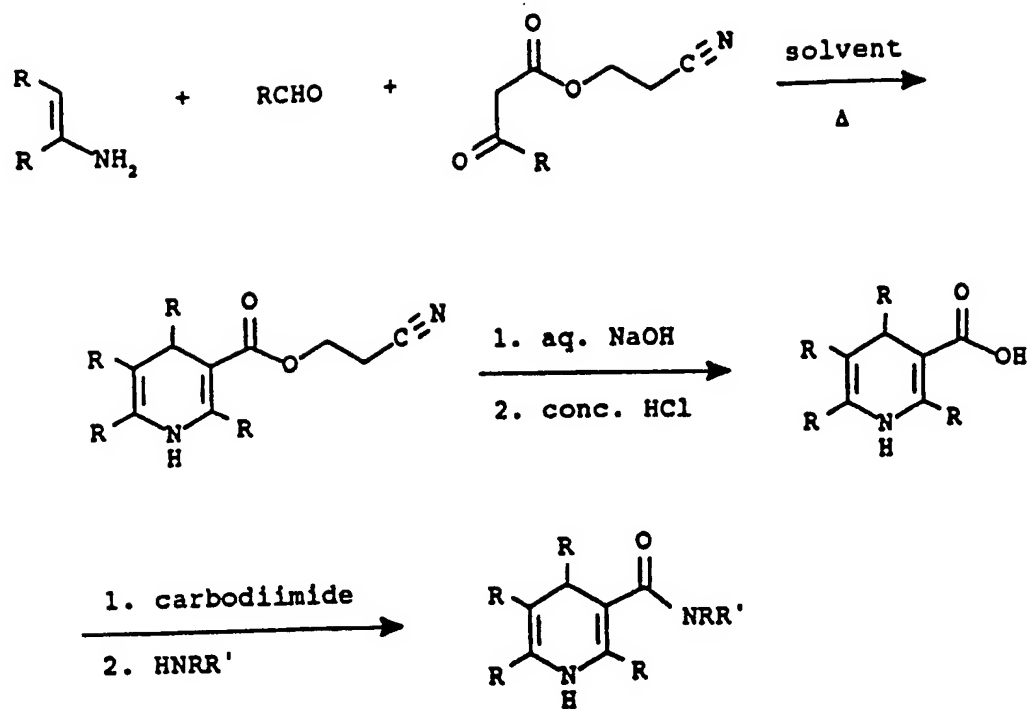


Figure 2

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Reaction Scheme 3 (Method C)

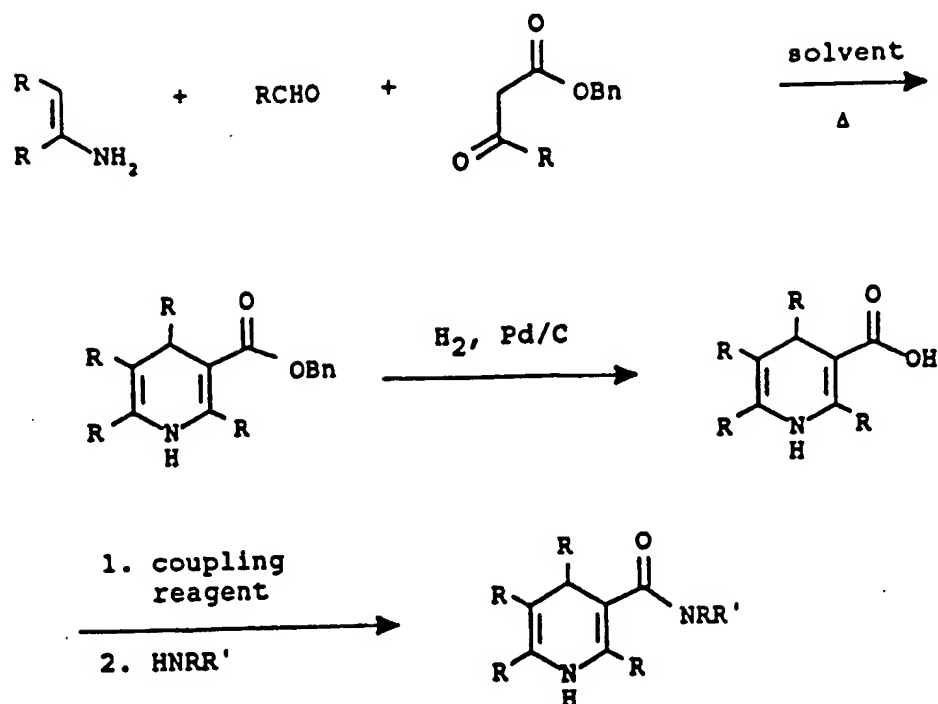


Figure 3

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Reaction Scheme 4 (Method D)

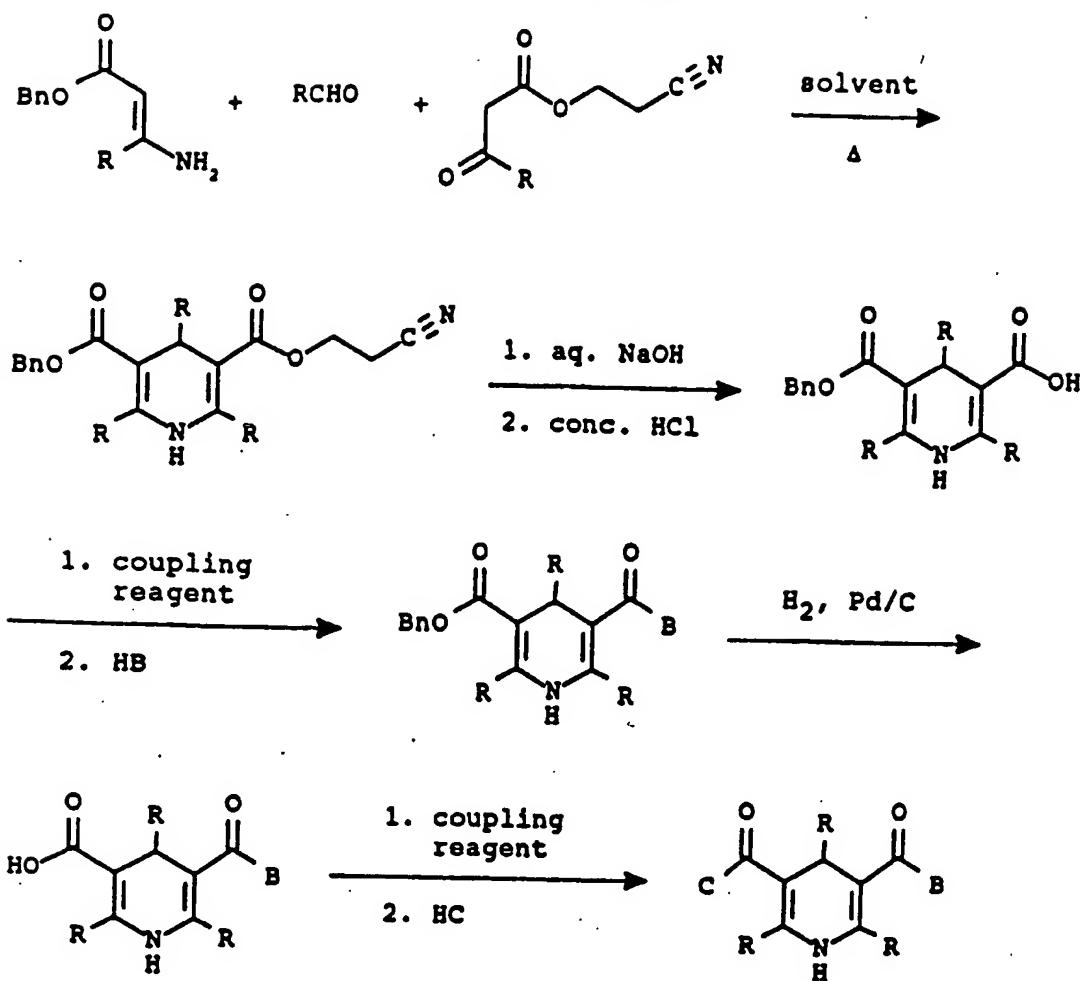


Figure 4

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